COVID-19 NEWSLETTER

The outbreak of SARS-CoV-2, the virus that causes COVID-19, has been categorized as a pandemic by the World Health Organization. This virus may cause additional challenges for people who are already vulnerable and particularly those who struggle with existing health conditions. There is no evidence yet about how people with Down syndrome (DS) are affected by COVID-19.

To better understand the risk and to inform appropriate recommendations to protect individuals with DS against COVID-19, the T21RS has launched an initiative in Europe, US, Brazil, and Spanish-Speaking Latin America.

Many of the T21RS members are now part of a T21RS COVID-19 workgroup that was assembled to better understand the risk and to inform an appropriate response. Our Clinical and Science & Society Committees have spearheaded the design and implementation of an international survey of COVID-19 in Down syndrome. This will be completed by carers and clinicians caring for individuals who have been diagnosed with COVID-19. T21RS is currently sending the survey links for distribution throughout the community. We will make our findings available at regular intervals to the entire Down syndrome community.

The survey is accompanied by an ongoing review of the relevant scientific and medical literature being undertaken by the Preclinical Committee of the T21RS. The goal is to better understand the potential roots of the vulnerability of DS individuals to viral respiratory infections in general, and whether this vulnerability translates into a specific vulnerability to COVID-19.

At T21RS, we are committed to conducting and supporting research needed to understand the following issues:

1) Whether individuals with DS are more vulnerable to SARS-CoV-2 infection
2) Whether those with DS are at an increased risk for complications arising in the context of SARS-CoV-2 infection
3) Whether there are atypical responses to treatments of COVID-19 among individuals with DS, including their response to future vaccines.

Review of relevant scientific and medical literature by the Preclinical Committee

The recent SARS-CoV-2 outbreak, which causes COVID-19, has proven to be particularly devastating for elderly individuals (>60 years old), especially for those with chronic medical conditions (i.e., hypertension, diabetes, cardiovascular disease, chronic respiratory disease and cancer). As of now, the SARS-CoV-2 virus infection has been confirmed in at least 1,904,566 persons worldwide and is responsible for at least 118,459 deaths, numbers that are expected to continue to rise in the coming weeks.

The fast spread of SARS-Cov-2 has outpaced the development of drugs with demonstrated ability to prevent infection or lessen its effects. Therefore, no drug therapy has been officially approved thus far. Small clinical studies and anecdotal accounts from clinicians have provided some preliminary evidence, but the evidence base is still in an embryonic phase, and much remains before it is shown which treatments are effective. Nevertheless, the U.S. based Food and Drug Administration (FDA) issued an emergency investigational new drug (eIND) use authorization for remdesivir (an anti-viral treatment originally used for Ebola infections) and for hydroxychloroquine (an old anti-malaria treatment) so that physicians can prescribe them. In addition, the FDA has issued an eIND protocol in which plasma collected from individuals who have recovered from COVID-19 can be delivered into critically ill patients in the hope that the antibodies to the virus will lessen disease severity. In Europe, many hospitals are combining hydroxychloroquine with azithromycin (an antibiotic with anti-inflammatory and possibly antiviral action). They have also used ivermectin, an FDA-approved anti-parasitic with anti-viral activity in vitro against SARS-CoV-2, and Tocilizumab, an anti-IL6 treatment used for reducing the virus- induced cytokine storm and deterioration of lung function in SARS-CoV2 severe pneumonitis. Many of these experimental treatments are associated with significant side effects. Decisions regarding initiation of treatment should always be balanced against potential risks. Very recently, several clinical trials, which are essential for defining safety and efficacy of anti-viral treatments, have been initiated (see https://clinicaltrials.gov/). The European Medicines Agency (EMA) has created a special task force to take quick and coordinated action for the development and authorization of safe therapeutics and vaccines against COVID-19.

Testing for SARS-Cov-2 positivity in symptomatic and asymptomatic at-risk individuals may be an efficient way to reduce mortality and the spreading of COVID-19 (http://www.uni- goettingen.de/en/606540.html). Nasopharyngeal samples and sputum are typically used to detect viral genome using RT-QPCR with a sensitivity of around 500 RNA copies. These tests can potentially be widely used in individuals with Down syndrome (DS). Just as in the general population, priority should be given to those presenting with any symptom related to COVID-19, such as fever, tiredness, dry cough, shortness of breath, aches and pains, sore throat, diarrhea, nausea, runny nose, loss of smell and/or taste. However, there have been difficulties in developing sufficient testing capacity in many countries. In addition, the false negative rate of these tests may also be an issue.

At T21RS, we are concerned about the potential impact of SARS-CoV-2 infection in individuals with DS. Our concern for those with DS is based on their higher prevalence for respiratory tract infections and immune complications, including increased incidence of periodontal disease, infectious, and autoimmune disease. The extent of immune impairment in DS can be substantial, including functional anomalies in a variety of immune cells (i.e., T- and B-cells, monocytes and neutrophils) that are of importance to both immune response and suboptimal antibody responses to vaccination.

T21RS COVID-19 survey workgroup

The Clinical and Science and Society committees of the T21RS have established a workgroup with input from experts and clinical interest group representatives from several affected countries. The workgroup has developed a protocol and designed two online REDCap forms to gather information from caregivers or clinicians. It is focused on understanding risk factors and treatments associated with outcomes in individuals with Down syndrome diagnosed with COVID-19. The survey has now completed IRB review, and has been translated into Spanish and Portuguese. It is also being translated into French and Italian. The first preliminary data check is due within the next week, after which data will be analysed and made available every two weeks.

Members of the workgroup include:

Stephanie Sherman, Emory University and co-chair, Clinical committee Alberto Costa, Case Western Reserve University, co-chair Clinical committee Mara Dierssen, Center for Genomic Regulation and past president of T21RS Andre Strydom, King's College London and T21RS president
Anne Sophie Rebillat, Lejeune Institute (Paris) and co-Chair, Science and Society Committee Maria Carmona Iragui, Sant Pau Memory Unit, Spain and Co-Chair Science and Society Committee
Stefania Bargagna, Fondazione Stella Maris, Italy
Guissy Sgandurra, Fondazione Stella Maris, Italy
Angelo Carfì, Fondazione Policlinico Universitario A.Gemelli, Italy
Diletta Valentini, Ospedale Pediatrico Bambino Gesu, Italy Andrew Nowalk, University of Pittsburg (Infectious diseases), USA
Anke Huels, Emory University (Environmental health and epidemiology), USA
Monica Lakhanpaul, University College London, and DSMIG-UK representative
Martin Gulliford, King's College London (Public health), UK
Nicole Baumer, Harvard University, USA and DSMIG representative
Ferran Sanz, Research Programme on Biomedical Informatics of IMIM-UPF, Spain
Miguel-Angel Mayer, Research Programme on Biomedical Informatics of IMIM-UPF, Spain
Rafael de la Torre, Consorci MAR Parc de Salut de Barcelona (Pharmacology), Spain
Coral Manso, Down Spain
Agustin Matias, Down Spain
Jesus Flórez, Fundación Iberoamericana DOWN 21
Maica Ortega, Hospital Universitario 12 Octubre (AGCPSM), Madrid, Spain

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Spanish COVID-19 workgroup actions

In Spain the COVID-19 workgroup already launched the Spanish version of the Clinicians and Family surveys created by T21RS on Friday April 10th along with the press release. The Spanish COVID-19 is formed by 20 professionals including epidemiologists, internal medicine clinicians, public health specialists, primary care doctors, data scientists, social scientists, and health specialists of Down syndrome Associations. We also liaised with key partners in the country, such as the country health and pandemic response authorities. The ethical clearance was obtained from the local IRB (CEIC, Parc de Salut Mar) and is now available for all the hospitals involved.

Methodology

The Spanish group prepared a country action plan with timeline plus roles and responsibilities and adapted the emails and survey to the national context, consulting with the local specialists and key stakeholders to ensure clarity, and applicability. We also established a data-collection methodology. The outreach to the Spanish and Latin American families and Associations has been coordinated with hospitals and families through DOWN Spain to minimize or avoid duplicated cases. Until now, around 50 cases have been identified and during this week, we will have the information updated in

REDCap for analysis.

Data Analyses

The Spanish workgroup has suggested that data collected with different participants can be assessed over time. A first analysis will be done within the first week, with the approximately 50 cases in Spain to ensure data quality, and provide first guidance on the recommended process and steps. This will also help establish suitable data formats to analyse data and produce visual representations that can be easily reviewed and understood by a wide audience. Repeated assessment of the same core variables allows analyzing changes in available interventions and treatments over time. It will also allow comparisons across countries if desired.

Members of the Spanish workgroup:

Centro Médico Barcelona Down de la Fundación Catalana Síndrome de Down (FCSD)
DOWN ESPAÑA
FIADOWN (Federación Iberoamericana de Instituciones para el síndrome de Down)
Fundación Iberoamericana DOWN 21
Hospital La Princesa, Madrid (Unidad de atención al adulto con SD)
Hospital del Mar. Instituto de Investigaciones Médicas IMIM, Barcelona
Research Programme on Biomedical Informatics of IMIM-UPF
Centro de Regulación Genómica, Barcelona
Hospital Niño Jesús, Madrid
Servicio de Neurología, Hospital de la Santa Creu i Sant Pau, Barcelona
Hospital Universitario 12 Octubre (AGCPSM), Madrid
Hospital Universitario Marqués de Valdecilla, Santander
Instituto Hispalense de pediatría de Sevilla

Testing COVID-19 in European research institutes

In France, following a ministerial decree, academic laboratories can be requisitioned to perform PCR tests for SARS Cov-2 detection. At the Paris Brain Institute (ICM), on the Salpêtrière Hospital site, we started a Covid19 testing unit in a confined lab level 3. The hospital lab is testing patients and we are starting helping with medical staff using mainly sputum, which are much easier to collect and have been shown to be as sensitive as nasopharyngeal samples (PMID 32235945). We collect sputum, inactivate them and treat for fluidity, extract RNAs and run one-step RT-QPCR following the protocol from the Pasteur Centre of Reference also on the WHO website. RNA extraction is the limiting step and today, using a 16xMaxwell automate, we can run 100 test and will have the possibility to use a 48xMaxwell automate if needed. We amplify two portions of the RNA polymerase from the virus and an additional human housekeeping gene (RNA polymerase) to check the quality of sampling on the iGENSEQ platform of ICM. Overall, we collect samples in the morning, run the RNA extraction and PCR and can deliver the results the same day or the day after. From reception of samples to results in a Redcap database, we have written all the procedures. We are working with the virology laboratory of the hospital in order to deliver results. It took us a couple of days to set it up, these recipes are like egg cooking for a chef and we will be happy to send those recipes to any lab wanting to participate in “test, test, test” as the President of the WHO said last March.
Dr. Marie-Claude Potier, Director of Research at CNRS, co-team leader at ICM.

In Spain, the Catalan Government (Generalitat de Catalunya) has launched the ‘Programa Orfeu’, a

massive coronavirus testing service on two research institutes of Barcelona. Researchers from Centre for Genomic Regulation (CRG) are running proofs of concept to implement, standardize and improve real time PCR and other protocols for efficient and reliable detection of viral RNA, to increase the number of tests and cheapen the cost. The idea is to run a relatively small number of tests at first, 500-800 per day, and slowly ramp up to 8 or 10,000 per day, helping the Generalitat reach its target of 170,000 tests in total by the end of May. Besides CRG provided RNeasy Kits for RNA isolation, gloves, lab coats and guanidine thiocyanate for tests at Catalan hospitals. Finally, CRG set up a public resource (https://biocorecrg.github.io/covid/) that collects all publicly available SARS-CoV-2 direct RNA sequencing datasets.
Dr. Mara Dierssen, Researcher at CRG, T21RS past president.

Join a webinar organized by The Matthew Foundation

The Matthew Foundation has organized a webinar on April 17th to help Down syndrome individuals and their families deal with some key issues during the COVID-19 outbreak. The association is working on doing a series of COVID-19 & Down Syndrome virtual events on topics that are top of mind to parents due to staying at home - i.e. Mental Health for parents, Mental Health for people with Down syndrome, therapies from home, etc.

Webinar Topics: Distance Learning/Managing School from Home and a Medical Overview due to COVID-19 (based on the document published by the consortium of DS organizations including T21RS) and the stay at home situation.
Date/Time: Friday, April 17 @ 5pm ET/2pm PT
Register: https://www.thematthewfoundation.org/covid-19.html

COVID-19 - The Matthew Foundation - Down syndrome research, inclusion, and employment
www.thematthewfoundation.org
COVID-19 & DS ONLINE VIRTUAL SERIES
Facebook: https://www.facebook.com/thematthewfoundationinc/

Presenters:
Chris Lemons, Assoc Prof of Special Education, Stanford University (frequent NDSC speaker)
Brian Chicoine, Medical Director, Advocate Medical Group Adult Down Syndrome Center (Adult)
Noemi Spinazzi, Medical Director, UCSF Benioff Children's Hospital Down Syndrome Clinic (Pediatrics)

Participate in the T21RS newsletter!

Mari Luz Montesinos, Eric Hamlett and Claudia Cannavo

Mari Luz Montesinos, Eric Hamlett and Claudia Cannavo are the Communication Work Group at T21RS. One of our missions is to coordinate this newsletter, and we need your ideas, pictures, comments... Please, email to mlmontesinos@us.es with your contributions, and, of course, follow T21RS on Twitter (@t21rs)