Project title

Combining German *in silico*-/Egyptian wet lab-expertise to model COVID19 immunological data

Abstract

Emergence of the SARS-CoV-2 infection in 2019 has limited the research exchange through travelling and pushed the scientific community world-wide to cooperate remotely. We all know how emergence of electronic communication means starting from e-mail in the 90s of the last century has converted the big world into a small village and contributed to gradually diminishing the barriers between countries. However, the challenges now are beyond exchanging ideas through e-messages. There is a growing need to allocate funding that promotes digital research exchange. Our German (Prof. Konrad Förstner; TH Köln) /Egyptian (Prof. Mahmoud Bahgat; NRC) collaborative network has thought of this ahead of the COVID-19 pandemic and addressed possibilities to utilize computational and information technology-based approaches to control infection. Through two successive renewed research stays in 2017 and 2019 MB has visited KF research institute at the ZB MED and the TH Köln where he received an extensive introduction on using open source computational tools to analyze and model big data. During the second stay MB learnt that KF research team is developing new data mining and computational tools to enhance extraction of all needed information for research and analyze data remotely. Here we plan to combine the wet lab expertise and infra structure of the Egyptian applicant at the NRC with the computational infrastructure and expertise of the German virtual host at the ZB MED and the TH Köln to model immunological data form infected subjects with SARS-CoV-2. The wet lab data generated by MB's team at the NRC include quantifying anti-SARS-CoV2-IgM, IgG and IgG subclasses in sera from asymptomatic individuals and individuals of differential disease severity. These data will be remotely analyzed using various computational bioinformatics and machine learning tools developed by KF's team at the ZB MED and the TH Köln with the aim to develop serology-based both disease severity and viral clearance prediction models.

Problem definition

Worldwide recent reports confirm that almost 96-97% of the infected humans with the novel corona virus (nCoV also known as COVID19) recover from the infection while 3-4% deaths of the infected subjects were reported (1-3).
Of the 96-97% human cases who recover, 80% recover spontaneously whereas 16-17% develop symptoms and undergo hospitalization using the standard recommended treatment protocols of the WHO (3).
The 80% human cases who spontaneously recover represents a very dangerous reservoir of the nCoV which represents a major risk factor for the disease transmission as they carry the virus without developing severe symptoms.
In fact estimating those who develop either mild or no symptoms and mount immune responses which manage to clear nCoV infection represents a very important aim as it will identify the exact percentage of people who are at real risk of developing disease upon infection and those who are naturally able to spontaneously clear nCoV.
This will help future levels of preparedness and decision making in terms of needs to hospitalization, therapy and vaccination.

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Relying on rapid antibody detection tests, my research group has recently published data from an Egyptian cohort which clearly demonstrated 1) the impact ofthe socioeconomic standard, gender, and age on both primary andsecondary immune responses to SARS-CoV-2 infection and, 2) heterogeneityin individualized human responses to the SARS-CoV-2infection, which sometimes is asymptomatic and at other times isassociated with a broad range of symptoms (4).

Aim of the work

To model immune responses to SARS-CoV-2 infection in sera from asymptomatic individuals and sera from individuals who developed a range of COVID19 typical symptoms. The immune responses results to be modeled in this study will be generated from qualitative rapid tests and quantitative ELISA assays.

Research plan

1. Consent will be filled by all participants of the study.
2. A questionnaire will be designed including age, gender, suffering of chronic diseases if any and type of received medications if any during the period of the nCoV outbreak, the reason of receiving these medications and developing of fever, coughing or any flu-like symptoms during the time of the outbreak.
3. Blood samples will be randomly collected from a minimum of 100 individuals representing various age groups and genders.
4. Sera will be separated from the individual blood samples and appropriately bio-banked.
5. The sero-prevalence of the anti-SARS-CoV-2IgM, IgG(both qualitatively and quantitatively) and IgG subclasses (quantitatively) will be tested in the individual samples using commercially available SARS-CoV-2 antigen-based immuno-diagnostic reagents.
6. The sero-prevalence of the immunoglobulin classes and subclasseswill be correlated with the presence/absence of typicalCOVID19 symptoms as well as the diseases severity.
7. The overall concluded prevalence of all studied immunoglobulin classes/subclasses will enable estimating the actual prevalence of the exposure to SARS-CoV-2 among various genders and age groups in the studied cohort and the percentage of the individualswho are able to spontaneously clear infection.
8. The German team will help in using various computational bioinformatics and machine learning tools to analyze the generated immunological results on the Egyptian side. This will also involve training Egyptian students and post-docs remotely (digitally) on how to use these tools.

Expected outcomes

1. Estimating the actual sero-prevalence of the exposure to SARS-CoV-2 infection in an Egyptian cohort using a panel of immunoglobulin classes and subclasses.
2. Estimating the percentage of individuals which can spontaneously clear SARS-CoV-2 infection.
3. Estimating the percentage of individuals at high risk of receiving SARS-CoV-2 infection and developing sever symptoms.
4. Guiding preparedness for future infection waves at the level of needs for hospitalization, medications and vaccination.
5. Development of immunology-based both disease severity and virus clearance prediction models.

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How the digital collaboration is planned

1. Online group meetings between the Egyptian and the German collaborators and their teams.
2. Online training of Egyptian junior researchers on, and giving them access to, established bioinformatics and machine learning tools in German institutes remotely.
3. Electronic exchange of generated wet lab raw data in Egypt and analyzed/modeled data in Germany.
4. Providing scripts, libraries and packages developed on the German side to be used to analyze data on the Egyptian side.

Advantage of the digital fellowship

With the known restriction on transfer of human samples according to Nagoya protocols, and in the light of the of restricted travel (exchange) due to the SARS-CoV-2 pandemic, generating funding schemes that support generating wet lab data in Egypt (Africa) and encouraging digital collaboration that allows giving Egyptian junior researchers access to, and training on, established bioinformatics and machine learning tools in German institutes remotely present a unique opportunity introduced by the AvH Foundation to enhance German-Egyptian collaboration.

Additional funding

Noteworthy, the wet lab work is receiving additional financial support from the National Research Centre (NRC) of Egypt. This support has started since 2020 and will end in July 2022. The received financial support while between August 2021 and July 2022 is 8333 EUR. This fund can be used only in buying consumable and reagents but cannot be used to pay personnel of to buy equipment. Of course the received fund through digital fellowship will be used to increase the number of the measured immunological parameters and to compare readout of qualitative to quantitative tools. It will also enable buying small laboratory instruments and paying staff costs which are not eligible from the NRC grant.

Budget breakdown for the whole duration of the fellowship (Calculated/ 6Months)

Consumables	Reagents	Small equipment	Staff costs	Total (EUR)
1500	**3500**	**6500**	**3500**	**150000**

Reference

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