March 24, 2020, New York.

Dear friends,

A number of inborn errors of immunity (IEIs) selectively underlie life-threatening viral diseases, including herpes simplex virus encephalitis, fulminant viral hepatitis, lethal cytomegalovirus primary infection, severe influenza pneumonitis, and others. In December 2019, a pneumonia due to a novel coronavirus (SARS-CoV-2) emerged in China, and quickly spread world-wide with an increasing number of cases and deaths. In populations naive to this new pathogen, there has been stunning inter-individual variability among infected individuals, ranging from asymptomatic infection to lethal coronavirus infectious disease-19 (COVID-19). Two groups are at high risk of severe disease: elderly people (>70 years) and patients with a pre-existing condition (including but not limited to cardiovascular and pulmonary diseases, diabetes and obesity, liver or kidney dysfunctions, and overt immunodeficiency). Only a small proportion of otherwise healthy, young people therefore fail to control SARS-CoV-2 infection.

In this context, we hypothesize that life-threatening COVID-19 in previously healthy individuals younger than 50 years can be caused by IEIs.

In collaboration with many colleagues in the field world-wide, including Helen Su, Luigi Notarangelo, and Stuart Tangye in particular, our project will tackle three specific aims:

1) to recruit otherwise healthy young patients with severe COVID-19 (and their family members when available).

2) to search for candidate disease-causing variants by whole-exome sequencing of patients and controls (including asymptomatic infected subjects).

3) to perform functional studies to characterize the products of the candidate variants biochemically, and to analyze the corresponding patients’ cells immunologically.

Our project should reveal the critical circuits involved in the pathogenesis of severe COVID-19, thereby paving the way for the development of novel preventive and therapeutic strategies.
The recruitment criteria are:

- Children or adults <50 years old
- Without risk factors, including but not limited to: HIV+, cardiovascular disease, obstructive lung disease, chronic liver dysfunction, chronic kidney dysfunction, malignancy, previous bone marrow or stem cell transplantation, immunosuppressive treatment, overt obesity or diabetes, etc.
- Diagnosed with SARS-CoV-2 by PCR
- Clinically diagnosed acute respiratory distress syndrome (ARDS) and/or encephalitis
- Admitted to intensive care unit (ICU) or equivalent facility

Please join our effort! We need whole blood, fresh or frozen, or genomic DNA from patients.

For all questions, please contact:

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