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484 SARS-CoV-2 full length spike protein for COVID-19 vaccine development and diagnostic testing

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RATIONALE: As of August 2020, the Centers for Disease Control and Prevention have reported >5.6 million cases and >175,000 deaths due to COVID-19 in the US. Our goal was to produce high quality SARS-CoV-2 proteins for vaccine development and diagnostic testing.

METHODS: Recombinant full-length spike protein was genetically engineered to have enhanced stability, expressed in CHO cells, and purified by affinity chromatography. Expression was validated by western blot. An ELISA was performed to evaluate binding of a commercially available anti-spike antibody to the recombinant spike protein. Purity was assessed by silver-stained SDS-PAGE and by relative peptide abundance using LC-MS/MS. COVID-19 positive patients' sera were tested for IgG reactivity to the spike protein. Mice were immunized with SARS-CoV-2 proteins.

RESULTS: The recombinant spike protein was found to be >95% pure by LC-MS/MS (peptide signal abundance) and silver-stained SDS-PAGE. Expression of the full-length spike was confirmed by western blot which showed a single band at ~140 kD, which was recognized by an anti-spike antibody. Ten COVID-19 positive patients' sera, but not negative controls, had high IgG reactivity to the spike protein (titers >1/10,000). Mice immunized with the spike S1 subunit had IgG reactivity to the full spike.

CONCLUSIONS: High quality SARS-CoV-2 spike protein was produced and used to develop an IgG antibody immunoassay. The purified spike protein did not react with COVID-19 negative patient sera and had high reactivity to COVID-19 positive patients. The pure and immunoreactive spike protein has applications in antibody testing and vaccine development.

485 Outcomes of SARS-CoV2 infection in STAT3 and PGM3 Deficiency

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RATIONALE: While SARS-CoV2 continues to spread globally, our understanding of the disease continues to be limited in patients with underlying immune dysregulation.

METHODS: Four subjects with known monogenic immunodeficiency with HyperIgE phenotype and confirmed or clinically suspected SARS-CoV2 infection were tele-interviewed to assess for symptoms, duration, severity and complications of illness.

RESULTS: Three patients had STAT3 deficient HyperIgE syndrome and one had PGM3 deficiency. All were on antimicrobial prophylaxis during SARS-CoV2 infection. 8-year-old male with PGM3 deficiency related lymphopenia, neutropenia, and reactive airway disease tested positive for SARS-CoV2 and experienced 2 days of low-grade fever and cough. 26-year-old male with STAT3 deficiency working in a high-exposure environment tested positive and experienced symptoms for 2 weeks including headache, myalgias, low-grade fever and dyspnea on exertion. He received additional antibiotics around day 7 of illness when his course worsened briefly. 45-year-old male with STAT3 deficiency, with exposure to confirmed positive family member, developed intermittent low-grade fever, chills, myalgias, severe fatigue, and dyspnea on exertion, lasting for 20 days. His 14-year-old daughter with STAT3 deficiency experienced 14 days of fatigue, low-grade fever, anosmia and ageusia. All 4 patients were

managed at home without requiring supplemental oxygen, hospitalization or residual complications.

CONCLUSIONS: Despite concern for worse outcomes for patients with immunodeficiency including HyperIgE syndromes, our patients exhibited favorable outcomes with relatively mild COVID-19 clinical course. This may underscore the absence of excessive immune response to SARS-CoV2 in this patient population; however, number of patients was limited, and more research is required to understand significance of these underlying diseases.

486 Immunodeficiency during COVID-19 pandemic: analysis of a 243 patients' cohort followed at a Brazilian tertiary hospital

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RATIONALE: COVID-19 pandemic raised doubts about susceptibility and disease prognosis of immunodeficient patients compared to general population. Our objective was to evaluate these patients' profile and their evolution during pandemic.

METHODS: Retrospective analysis of 243 immunodeficient patients' medical records from March-July 2020. We evaluated socioeconomic conditions, adherence to social distancing, symptoms and type of immunodeficiency and comorbidities. Diagnosis was established through symptoms and positive SARS-CoV-2 PCR.

RESULTS: Most were women (58%), mean age 42.3y. The majority presented COVID (48.2%), followed by IgA deficiency (14.8%), agammaglobulinemia (4.1%). Some presented secondary immunodeficiency (14.4%). Comorbidities: bronchiectasis (22.6%), asthma (20.2%), COPD (9.5%), SAH (17.7%), obesity (14%), diabetes (7.8%) and cardiovascular diseases (5%). COVID-19 was confirmed in 10(4.1%) patients, of which 55.6% had positive IgG. About housing, 94.2% lived in the city, 72% in houses, with an average of 6.3 rooms and 3.1 residents/household. During pandemic, patients left home on average 7 times/month and 93.4% used mask, 63.4% used their own car, 23.9% used public transport. Those infected with SARS-CoV-2 had a higher mean of visitors compared to total cohort (2.4x1.4), lived more in apartments (50% x 27.6%), left home more often (8.8x7.0 times/month) and were more obese (60% x 14%)

CONCLUSIONS: Lower percentage of immunodeficient patients infected with COVID-19 (4.1%) was observed compared to that in general population of the city of São Paulo (11%), possibly due to greater isolation and fear of being contaminated. Those infected were less adherent to preventive measures and had higher incidence of comorbidities (obesity) related to worse prognosis of COVID-19.