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Pre-existing T-cell immunity to SARS-CoV-2 in unexposed healthy controls in Ecuador, as detected with a COVID-19 Interferon-Gamma Release Assay

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ABSTRACT

Background: Studies of T-cell immune responses against SARS-CoV-2 are important in understanding the immune status of individuals or populations. Here, we use a simple, cheap, and rapid whole blood stimulation assay - an Interferon-Gamma Release Assay (IGRA) - to study T-cell immunity to SARS-CoV-2 in convalescent COVID-19 patients and in unexposed healthy contacts from Quito, Ecuador.
Methods: Interferon-gamma (INF-γ) production was measured in the heparinized blood of convalescent and unexposed subjects after stimulation for 24 h with the SARS-CoV-2 Spike S1 protein, the Receptor Binding Domain (RBD) protein or the Nucleocapsid (NP) protein, respectively. The presence of IgG-RBD protein antibodies in both study groups was determined with an "in-house" ELISA.
Results: As measured with INF-γ production, 80% of the convalescent COVID-19 patients, all IgG-RBD seropositive, had a strong T-cell response. However, unexpectedly, 44% of unexposed healthy controls, all IgG-RBD seronegative, had a strong virus-specific T-cell response with the COVID-19 IGRA, probably because of prior exposure to common cold-causing coronaviruses or other viral or microbial antigens.
Conclusion and Discussion: The high percentage of unexposed healthy subjects with a pre-existing immunity suggests that a part of the Ecuadorian population is likely to have SARS-CoV-2 reactive T-cells. Given that the IGRA technique is simple and can be easily scaled up for investigations where high numbers of patients are needed, this COVID-19 IGRA may serve to determine if the T-cell only response represents protective immunity to SARS-CoV-2 infection in a population-based study.

Introduction

The immune response to SARS-CoV-2 infection involves not only antibody production, but the infection also triggers a T-cell response in patients (Lipsitch et al., 2020, Ni et al., 2020). In general, the determination of the presence and magnitude of a specific memory T-cell response to this coronavirus infection is performed with an ELISPOT assay by establishing the number of lymphocytes that produce IFN-γ after stimulation with disease-specific antigens or peptides (Ni et al., 2020, Pai et al., 2014, Abate et al., 2013, Braun et al., 2020, Grifono et al., 2020, LeBert et al., 2020, Sekine et al., 2020). For this technique, peripheral blood mononuclear cells (PBMCs) are isolated from fresh heparinized blood by density-gradient centrifugation; the secretion of cytokines by individual T-cells is quantified by microscope or with a special apparatus– the ELISPOT plate reader. The ELISPOT assay is a "for research laboratories only" technique that is highly laborious, technically demanding, relatively expensive, and cannot easily be used in a clinical laboratory or be applied in population-based studies. Due to the cost, infrastructure, and the laboratory

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