MEXICAN HUMAN LEUKOCYTE ANTIGEN ALLELES MIGHT PREDICT CLINICAL OUTCOME IN SARS-CoV-2 INFECTED PATIENTS

Country border lines are illusory and do not restrain the spread of pathogens. For instance, the US has now become the epicenter of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, but just South of its border, in Mexico, confirmed cases have only surpassed a thousand patients, and fatalities are less than a hundred. Such drastic differences replicate worldwide, with no merit due to health-care policies, but probably to ancestry and genetics.

Human leukocyte antigen (HLA) genes dictate the immune response to pathogens. Interestingly, HLA genes are the most polymorphic in the human genome and are non-randomly inherited as conserved blocks. The distribution of HLA alleles is determined by ancestry and natural selection through infectious diseases.

The immunogenetics of the Mexican population has been shaped by the infectious pandemics of the 16th century that killed more than half of the Native population¹ and a highly heterogeneous combination of Amerindian, Caucasian, and African HLA haplotypes². Thus, the immunogenetics of the Mexican population has stirred great interest. Moreno-Estrada et al.³ demonstrated that Mexican Mestizos can be genetically stratified into substructures concordant with indigenous ancestry, and these groups can be as genetically differentiated as Asians are from Europeans, along with considerable differences in biomedical traits.

The progression from a viral infection to clinical disease, with varying degrees of severity, is determined by a complex interaction between the virus and the host immune system. Specific HLA alleles favor antigen presentation of immunodominant viral epitopes and clearance of the infection, while others impair peptide presentation, mount a weak immune response, and are unable to eradicate the infection⁴. Studies on HIV/AIDS have consistently corroborated such correlation: among untreated patients with almost insignificant viral loads, or “elite” responders, the HLA-B*57 allele is *significantly increased* compared to non-controllers⁵, which represents an interesting paradigm. Hence, it is of utmost relevance to analyze the HLA haplotypes of patients capable of mounting an effective immune response against the SARS-CoV-2 and compare them with those who develop severe manifestations.

Our research group has just begun collaborating in a project aimed to analyze the HLA haplotypes of mild, severe, and fatal cases of SARS-CoV-2 infection in Mexico. This study will potentially provide the groundwork to translate the immunogenetics discipline into infectology, epidemiology, and public health, whereby impacting on health-care policies tailored for the Mexican population that in the face of future pandemics might prioritize genetically susceptible individuals.

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Received for publication: 03-04-2020
Approved for publication: 04-04-2020
DOI: 10.24875/RIC.20000135