Analysis of the Human Leukocitary Antigen (HLA) system distribution in the Brazilian population.


Abstract
This project aims to analyze the HLA alleles frequency in the Brazilian population. We used DNA samples of 36 Brazilians subjects to sequence genes of the HLA class I (HLA-A, -B and -C) and class II (HLA-DQA1, -DQB1, -DPB1 and -DRB1, 3, 4 and 5) using next-generation sequencing (NGS). The FASTQ data generated by sequencing were analyzed by the TruSight Assign HLA (Illumina) software. The data generated in this study will be made publicly available in the BIPMed project (www.bipmed.org), so it can be used as a reference for further studies in the Brazilian population.

Keywords: HLA system, Next-generation sequencing, Allelic frequency.

Introduction
The Human Leukocyte Antigen (HLA) genes are associated with infectious, autoimmune, psychiatric diseases and susceptibility to cancer. HLA genes are divided into class I, II and III and are in a highly polymorphic chromosomal region (6p21.3), resulting in allelic variation among different populations. A database of control individuals with the same genetic background is required for studies of HLA association with disease. Therefore, the construction of an HLA frequency database will be helpful for future studies that aim to understand better the role of HLA in drugs reactions and to investigate autoimmune diseases. Our goal is to determine the HLA allelic frequency on healthy subjects from the southeast region of Brazil using next-generation-sequencing. We have performed our study with 36 healthy individuals. We used the HLA TruSight v2 Illumina kit to prepare HLA amplicons of class I HLA genes (HLA-A, -B and -C) and class II HLA genes (HLA-DPA1, -DPB1, -DQA1, -DQB1 and -DRB1, 3, 4 and 5). These libraries were subsequently sequenced in an Illumina equipment. Data generated were analyzed using TruSight Assign HLA (Illumina) software.

Results and Discussion
The “classical” HLA genes class I and II are the most studied, with several alleles already reported. However, the non-classical genes are less polymorphic, have low expression levels and their roles are not well described yet. Therefore, our project focused only in the class I and II HLA genes (HLA-A, -B, -C, -DPA1, -DPB1, -DQA1, -DQB1 and -DRB1, 3, 4 and 5). The frequency of the most prevalent alleles can be visualized in Figure 1. The most common alleles were A*02:01:01 (37%), A*01:01:01 (18%), A*30:02:01 (11%), B*51:01:01 (25%), B*18:01:01 (22%), C*04:01:01 (24%), C*07:01:01 (21%), C*05:01:01 (16%), DPA1*01:03:01 (74%), DPB1*01:04:01 (30%), DPB1*02:01:02 (30%), DQA1*01:01:01 (20%), DQA1*05:01:01 (18%), DQB1*02:01:01 (19%), DQB1*03:01:01 (19%), DQB1*06:03:01 (15%), DRB1*03:01:01 (23%), DRB1*07:01:01 (23%), DRB3*02:02:01 (50%), DRB3*01:01:02 (28%) and DRB4*01:03:01 (81%).

Unexpectedly, HLA-DRB5 alleles were found only in three subjects (all individuals have the HLA-DRB5*01:01:01 allele).

Figure 1. Graphics showing allele frequencies of the HLA genes studied.

Conclusions
We expect that the results of this study will be used to evaluate genetic differences between populations and to investigate the molecular etiology of autoimmune disorders as well as abnormal drug reactions mediated by the immune system.

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