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## Analysis of the distribution of alleles of the Human Leukocyte Antigen (HLA) system in Brazilian population.

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### Abstract

Genes of the Human Leukocyte Antigen (HLA) system are associated with infectious, autoimmune and psychiatric diseases and cancer susceptibility. These genes have high level of polymorphism and present important diversity among different populations. To identify and relate HLA alleles with specific phenotypes, it is necessary to compare with a reference database of control individuals from the same population of origin of the patient sample studied. However, there are no HLA-reference databases for the Brazilian population. Therefore, we aim to determine HLA-allele frequencies of control individuals from the Brazilian population for class I genes of HLA-A, -B and -C, and for class II genes of DPA1, DPB1, DQA1, DRB and DQB1. These results will be of paramount importance for further studies in our population

### Key words:

HLA system, Genotyping, Distribution of alleles.

### Introduction

The HLA-system is divided into three classes: I, II and III. The first two are similar in structure and function, coding for glycoproteins that act presenting antigen to T cells<sup>1</sup>. HLA class III genes encode molecules regulating humoral immunity and inflammatory reaction<sup>2,3</sup>. Class I genes encode the classic HLA-A, -B and -C molecules, while class II genes encode HLA-DR, HLA-DQ, HLA-DP, HLA DM and HLA-DO. The high level of polymorphism of the HLA-system genes is considered a selective advantage maintained by heterozygotes, increasing immune reaction against pathogens<sup>4</sup>. Copy Number Variants (CNV), duplications, inversions, translocation and SNP-mutations in the HLA-system are believed to be involved in the susceptibility of more than a hundred diseases<sup>4,5</sup>. Therefore, it is very important to determine the distribution HLA subtypes in control population in order to carry out association studies aiming to investigate the relationship between HLA alleles and disease<sup>6</sup>.

### Results and Discussion

We will determine HLA alleles in a group of 300 healthy individuals of the Brazilian population. Genotyping will be accomplished using the HLA sequencing panel TruSight v2 (Illumina®), or a similar one depending on the standardization experiments. DNA libraries will be prepared by isolating and amplifying 11 specific loci of the HLA-system. Subsequently, DNA-libraries will be sequenced on an MiSeq (Illumina®) platform.

### Conclusions

We are currently working on the standardization of DNA-sequencing procedures in order to amplifying class I genes: HLA-A, HLA-B and HLA-C, and: class II genes HLA-DPA1, HLA-DPB1, HLA-DQA1, HLA-DRB and HLA-DQB1.

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<sup>1</sup> Benacerraf, B. Role of MHC gene products in immune regulation. *Science*. 1981; 212: 1229–38.

<sup>2</sup> Bayley, J.P.; Ottenhoff, T.H.; Verweij, C.L.; Is there a future for TNF promoter polymorphisms?. *Genes Immun*. 2004; 5: 315–29.

<sup>3</sup> Vandiedonck, C.; Beaurain, G.; Giraud, M.; et al. Pleiotropic effects of the 8.1 HLA haplotype in patients with autoimmune myasthenia gravis and thymus hyperplasia. *Proc Natl Acad Sci USA*. 2004; 101: 15464–9.

<sup>4</sup> Vandiedonck, C.; Knight, J.; The human Major Histocompatibility Complex as a paradigm in genomics. *Brief Funct Genomics*. 2009; 8(5): 379–394

<sup>5</sup> Amstutz, U.; Ross, C.; Castro-Pastrana, L.; et al. HLA-A\*31:01 and HLA-B\*15:02 as genetic markers for carbamazepine hypersensitivity in children. *Clin Pharmacol Ther*. 2013; 94: 142–9.

<sup>6</sup> Pillai, N.E. et al. Predicting HLA alleles from high-resolution SNP data in three Southeast Asian populations. *Hum. Mol. Genet*. 23, 4443–4451 (2014).