CREATION OF A NATIONAL BIOBANK OF INDUCED PLURIPOTENT STEM CELLS WITH 64% COVERAGE OF THE BRAZILIAN POPULATION

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Introduction: Organ transplantation is a reality in Brazil, with approximately 14.352 transplants performed in 2024. Despite the significant number of surgeries, the waiting list remains extensive, with over 60,000 people awaiting organ transplants in the country[1,2.] Alternatives to reduce this waiting list and increase the number of grafts are necessary, and the discovery that it is possible to reprogram adult cells to an embryonic stage by Yamanaka[3,4], so-called induced pluripotent stem cells (iPS), could be a solution to the organ transplant. Genotyping of the human leukocyte antigen (HLA) and identification of cells in triple homozygosity at the HLA-A, ~B, ~DRB1 *loci* and quintuple homozygosity at the HLA-A, ~C, ~B, ~DRB1, and ~DQB1 *loci* can be used for iPS generation and allows the creation of a bank of homozygous cells[5] that may be compatible with a large portion of the population for the clinical use of these cells. With this purpose, we sought to carry out the mapping of HLA-homozygous individuals and the collection of cells from these individuals to create the national iPS biobank. For Brazilian population immunological coverage, statistical data shows that 559 homozygous haplotypes are sufficient to cover 95% of the population[6]. Therefore, this project aims to create an iPS biobank that can genetically cover significantly the Brazilian population.

Objective: Create a national triple homozygous iPS biobank representative of the Brazilian population for therapeutic and research purposes.

Methods: Peripheral blood samples from triple- and quintuple-homozygous donors were collected for isolation, processing, and cryopreservation of mononuclear cells. Additionally, the DNA from these samples was extracted for HLA typing in high resolution via massive parallel sequencing. For iPS generation, mononuclear cells may be expanded and subjected to reprogramming factors. Six cell lines were characterized, and quality control were performed throughout the process.

Results: Recruitment has been conducted via telephone contact with all potential eligible donors for the project. The biobank collected 295 registered samples, with 270 confirmed triple homozygous typings, gathered from six different municipalities. . iPS cells from six distinct cell lines were generated, with the most frequently collected haplotypes being four triple homozygous and two quintuple homozygous. The number of haplotypes collected allows for approximately 64% coverage of the Brazilian population.

Discussion: One of the primary challenges encountered during the project's execution was establishing contact with potential donors. Many available contacts were outdated, and in several cases, communication could not be established due to individuals' unavailability. Nevertheless, the biological collection has resulted in a bank of 270 A~B~DRB1 triple homozygous cell samples, providing coverage for approximately 64% of the Brazilian population. Therefore, this biobank is a rich and

promising resource with great potential for scientific research and possible clinical applications.

Conclusion: To achieve broader population coverage, it's necessary to extend the sampling across the entire national territory. However, the biobank currently holds a rich collection of samples that enables further studies on the clinical applications of iPS technology.

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