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SEROLOGICAL VERSUS MOLECULAR CHARACTERIZATION OF CLASS II HLA FOR RECIPIENTS AND DONORS OF BONE MARROW TRANSPLANTATION

THESIS

Submitted in Partial Fulfilment of the
MD Degree
In

Clinical Pathology and Oncologic Laboratory Medicine and Hematologic Malignancies

By

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Abstract

The choice of a properly matched donor is the first most important task in bone marrow transplantation. HLA class II DRB* 1 proved to be the most important factor in determining the degree of graft rejection and graft versus host disease. One hundred and thirty five cases were subjected to different DRB* 1 typing techniques of varying levels of resolution. Comparative serological versus molecular typing was available for 35 cases , where 20% of results were discordant . This is due to cross reactivity and lack of sensitivity and specificity of the serological method . PCR-SSOP was applied using 2 comparative kits, INNO-LiPA kit (32 probes) was used for cases while Amplicore Roche kit (20 probes) was used for 67 cases. INNO-LiPA gave better resolution at both the haplotype and allele levels. Using SSOP (INNO-LiPA) commercial kit, single allele (high resolution) could be identified in 28 occasions in certain haplotype combinations and in DRB1*0701 and *1001 being single allele. Single allele was identified in 56 other haplotypes representative of most DRB1 specificities starting by INNO-LiPA followed by a modified PCR-RFLP making advantage of the commercial kit complemented by a limited number of specific primers and restriction enzymes. For class II, serological typing is not anymore the method of choice; DRB1 has to be molecularly characterized. Commercially available kits depending on SSOP give an intermediate level of resolution, to reach a high level a complementary modified PCR-RFLP was introduced. With the final aim of applying this technique to different donor selection protocols, whether for siblings, family members, unrelated donors or cord blood. This is a practical economic and simple technique which could be a reasonable substitute for the sequence-based typing when it is not available, however, it can not detect new described alleles.

Keywords: HLA class II DRB1 typing, PCR-SSOP, PCR-RFLP