



Virtual Crossmatch in the Context of Kidney Transplantation



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Abbreviations: VXM: Virtual Crossmatch; CDC: Complement Dependent Cytotoxicity; FCXM: Flow Cytometric Crossmatch; HLA: Human Leukocyte Antigen; SA: Single Antigen; DSA: Donor Specific Antibodies; MFI: Mean Fluorescence Intensity

Introduction

The patient survival is strongly influenced by the presence of DSA [1-5]. Currently, Virtual Cross Match (VXM) has been used to predict the real crossmatch results by Complement-Dependent Cytotoxicity (CDC) and Flow Cytometry crossmatch (FCXM) [6-10]. VXM compare donor HLA antigens with anti-HLA antibodies in recipient serum. The antibodies are detected by the Single Antigen (SA) assay, in which each bead is coated with a single HLA specificity, detecting the precise anti-HLA antibodies and their levels, allowing predict reactions against donor HLA antigens. However, SA assays has some limitations that can, difficult the VXM interpretation [11]. The SA assay show higher sensitivity whereas the CDC and FCXM are specific against donor HLA molecules, which suggests that methods may be complementary [7-10].

Discussion

The high sensitivity and specificity of the SA assay in the detection of DSAs allows for the performance of a virtual crossmatch, although many studies have demonstrated that virtual crossmatch has limited value in predicting the result of the crossmatch, because the SA assay has some disadvantages [10-15]. The concentration of HLA in beads may vary due to differences in the binding of HLA molecules to the bead surface, not representing the antigens present in graft tissue. SA assay is not donor specific and use purified HLA antigens bound to the beads, thus possibly distorting molecular conformation during the binding process and can provide a false positive result and SA bead panel cannot include rare HLA antigens [11-16]. Further, the HLA typing of donors performed on HLA-A, B, C, DR, DQ and DP loci shows the importance for the accurate assessment of the presence of DSA. Previous studies have demonstrated that DSA with median fluorescence intensity (MFI) ≥ 5000 correlate with FCXM and CDC positive, this cut off has

been commonly used in VXM[10,12]. However, some publications indicate that MFI, although is a numerical value, should not be used to quantify antibodies [11,17].

In this context, use a fixed cutoff for VXM may not be an adequate option, in fact there is no single value that corresponds to a threshold above or below which contraindicated the transplantation without risk [18]. VXM allow for the quantification of antibodies by MFI and patient stratification by risk groups (sensitization), therefore it should be used with aim of favoring hyper sensitized patients and not excluding them from being tested in real crossmatch (CDC e FCXM) [19], which suggests that the methods are complementary[8,20,21].

Conclusion

The antibodies detection techniques are increasingly sensitive and specific, however, the excess of information can difficult to interpretation results and make decisions. The analysis of the techniques together (CDC, FCXM and VXM) as well as the patient historic, can provide important information to transplantation even on the presence of DSA and may help in the post-transplant patient monitoring and in immunosuppressive strategy.

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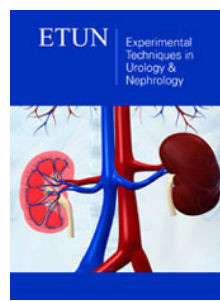
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