

## Letter to the Editor

# Biomarkers: A Sword for Achieving Long-Term Graft Survival

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Although solid organ transplantation has been greatly advanced, achievement of permanent acceptance of transplants remains a critical challenge in clinic owing to various clinical confounders such as virus infection, nephrotoxicity, etc [1]. Earlier identification of allograft function and status will guide physicians to undertake preemptive treatments including alteration of use of immunosuppressants, which will minimize the risk of allograft rejection episodes and subsequently allograft dysfunction even failure [1,2]. Individualized biomarkers for transplant recipients will lead to personalized therapies in the end.

Indeed, many efforts have been made to identify suitable and applicable biomarkers. However, standardization of those biomarkers is not sufficient among different multiple international transplant centers. Probably categorization of various biomarkers is required since they are detected from different settings of transplanted organs. For instance, it is interestingly observed that the biomarkers patterns for living and non-living kidney grafts are disparate in practice. This insult may be caused by different transplant outcomes. In general, outcome of living donors is much better than that of non-living donor organs [1,2]. Delayed graft function (DFG) can be frequently observed owing to lower quality of organs such as donors from cardiac death (DCD) and donors from brain death (DBD) [1,2]. Our previous study exhibited that weight difference between donor and recipient could affect primary graft function, resulting into DFG [3]. The pro-inflammatory cytokine interleukin-6 (IL-6) stemming from donor organ was counted for this effect. Neutralizing critical IL-6 may improve the graft function recovery [3].

Not only genes but proteins and cells may act as effective biomarkers for predicting graft status [2]. From the viewpoint of

practical diagnostic techniques, repetitive sampling from peripheral blood or urine is instructive in dynamic and continuous monitoring graft function [1,2]. Our own study displayed that peripheral Toag-1 (tolerance associated gene-1) gene expression was closely associated with intragraft settings (Weihua Gong, et al., unpublished data) in the rat kidney transplant model. In addition, peripheral frequency of MDSCs (myeloid-derived suppressor cells) reported by our group could be utilized to predict transplant outcome in the mice pre-sensitized transplant model [4]. However, cautions should be taken to extrapolate our data to different transplant models, implying that setting-specific identified biomarkers are normally confined to the referred scenarios.

Combined use of various biomarkers is strongly suggested as the single may not provide comprehensive information on transplant settings. Our own studies demonstrated that neither peripheral nor intragraft Foxp3 gene expression level could predict long-term allograft outcome. Nevertheless, combination of peripheral Foxp3 and alpha-1,2-mannosidase was capable of monitoring graft status and dysfunction, which will benefit clinicians taking measures to prevent further irreversible organ damage even rescue of graft dysfunction [2].

As the translational medicine is highly developing, a considerable number of transplant-associated biomarkers are being identified including living or non-living biomarkers. The ideal biomarkers should at least meet a need of sensitivity and specificity under various clinical confounding factors. The validation and standardization of those biomarkers is becoming a new challenge for clinicians. International collaborations are required to prove the predictive power of those identified biomarkers. All these work will significantly advance the rapid development of allograft survival.

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