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Evaluation of Digital PCR for Monitoring of Acute Rejection in Kidney Transplantation

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Background: Early detection and proper management of rejection in transplantation is a crucial for long-term health. The current standard ways to monitor rejection are serial serum creatinine measurement, although some programs supplement with surveillance graft biopsy. Donor-derived cell-free DNA (cfDNA) from grafts in plasma and urine of recipient is potential biomarker to detect acute rejection in transplant patients.

Methods: In this study, we evaluated the digital PCR (dPCR) system to monitor the graft status in kidney transplant patients using single nucleotide polymorphism (SNP)-based donor DNA detection in plasma or urine samples. Initially, we compared the performance of 3 different dPCR systems (QX200, RainDrop and QuantStudio 3D). We found that Bio-Rad QX200 has best performance to detect DNA using SNP markers in terms of accuracy and sensitivity.

Results: We found that at least 24% of highly polymorphic SNP markers used in human identification can be used as informative DNA markers to detect donor DNA in transplant patients. Furthermore, we found that all autosomal SNP, sex-determining SNP and mitochondrial SNP are good DNA markers to detect cfDNA in plasma or urine DNA samples. Finally, we assessed whether the measurement of donor-derived cfDNA using dPCR system can accurately monitor the clinical conditions of acute rejection in kidney transplantation using a total of 34 patients' plasma or urine DNA samples isolated at multiple time points after transplantation. We found that donor DNA percentage was almost undetectable in plasma DNA samples due to high background of recipient's DNA from recipients' cells, whereas high donor DNA percentage was measured in urine DNA samples, indicating that urine DNA is a good source of cfDNA for kidney transplantation monitoring. However, both total positive DNA counts and donor DNA percentage could not distinguish the clinical conditions of transplanted patients due to high inter-patient variations.

Conclusion: Our results indicate that non-invasive dPCR system is not an accurate screening method at this point to monitor the clinical conditions in kidney transplant patients.

Keywords: cell-free DNA (cfDNA), digital PCR(dPCR), Kidney Transplantation, single nucleotide polymorphism(SNP)