Viracor | Eurofins Clinical Diagnostics

Viracor TRAC™ Kidney dd-cfDNA Testing

Transplant Rejection Allograft Check (TRAC), donor-derived cell-free DNA (dd-cfDNA)

TEST CODE: 30876

CPT CODE: 0118U

Contact Client Services at 1-800-305-5198 prior to ordering, this test requires special tubes for collection.

Clinical Utility

The Viracor TRAC™ (Transplant Rejection Allograft Check) Kidney donor-derived cell-free DNA (dd-cfDNA) assay is designed to utilize a noninvasive liquid biopsy to monitor the percentage of dd-cfDNA in transplant recipient plasma post-transplant using next generation sequencing (NGS).

About Kidney Transplant*

Kidney transplant accounts for the highest number of transplants per year. A transplant may involve just one, or sometimes both kidneys. Unlike some other solid organ transplants, kidney transplant is one that can be supplied by a living donor, related or un-related. Renal disease or failure, resulting in the inability to remove waste and maintain balance of electrolytes, can be acute or chronic. If it cannot be treated the patient must be put on dialysis, and/or transplanted. The current 1 year survival rate for those with a first time renal transplant is at 97.1%, falling to 86.3% in 5 years post-primary transplant. The 2016 Annual Report published by OPTN/SRTR summarizes allograft survival specifically in kidney transplant.

About Transplant Rejection and dd-cfDNA

The current standard method of allograft rejection diagnosis and surveillance is by organ biopsy, which is an invasive technique that suffers from high cost and multiple potential serious complications for the patient. Biopsies may also be inconclusive and lead to adverse treatment decisions. Recently, quantification of dd-cfDNA (by NGS methods) in a transplant recipient's plasma has been developed to non-invasively monitor and diagnose organ rejection in transplant recipients.

Research has shown that donor-derived cell-free DNA (dd-cfDNA) found in a patient's plasma may be used as a liquid biopsy marker for identifying solid organ transplant rejection. Donor-derived cell-free DNA is released when the donated organ is attacked by either antibody or cell-mediated rejection processes. While the exact mechanism of action resulting in the circulating dd-cfDNA is not known, some researchers have speculated it could be produced by apoptosis, necrosis or active secretion. Regarded as a potential universal molecular biomarker, the concept of dd-cfDNA is being applied to several different solid organ transplant recipient populations. Not only is the method noninvasive, but the method has the ability quantify the percentage of cell-free DNA post organ transplant.

About Viracor TRAC™ dd-cfDNA

The Viracor TRAC™ dd-cfDNA test enables providers to detect solid organ transplant rejection using plasma isolated from Streck BCT tubes, providing essential information in a non-invasive way, which may be useful in the diagnosis of solid organ transplant rejection. This test utilizes a bioinformatics pipeline that analyzes NGS and genome-wide recipient genotype data to determine the percentage of dd-cfDNA present, which strongly correlates with allograft injury due to rejection. The licensed algorithm accurately quantifies the donor-derived fraction of cell-free DNA without need for donor genotype information, even when the donor is closely related (e.g., sibling kidney donors). The design of this test also enables the determination of dd-cfDNA concentrations over a much wider dynamic range than currently possible with other methods.

*Based on OPTN data as of March 1, 2019
https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/

Turnaround Time

4-6 days business days from receipt of specimen.

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Specimen Requirements

- Ship Monday through Friday. Friday shipments must be labeled for Saturday delivery. All specimens must be labeled with patient's name, collection date and time.
- **CAUSES FOR REJECTION:** Whole blood frozen, specimens beyond their acceptable length of time from collection as listed in the specimen handling, or specimen types or containers other than those listed.

Specimen Type	Volume	Special Instructions
Whole Blood	10 mL	• Collect 10 mL whole blood in a Streck cell-free DNA BCT. Tube must be completely full to maintain proper ratio of blood to anticoagulant. • For best results, a 21G or 22G needle is advised. Slower fill times may be observed when using a smaller gauge needle. • Regarding order of draw: Cell-Free DNA BCT can be drawn after EDTA tubes (purple top) and before the Glycolytic inhibitor tubes (grey top). If a Streck tube immediately follows a heparin tube, collect an EDTA tube first as a waste tube prior to collection in Cell-Free DNA BCT. When using a winged (butterfly) collection set for venipuncture and the Cell-Free DNA BCT is the first tube drawn, a non-additive or EDTA discard tube should be partially drawn first in order to eliminate air or "dead space" from tubing. • After venipuncture, it is critical to mix tubes thoroughly by inverting the tube 8-10 times end-over-end immediately after collection. • Ship the Streck tube via ambient shipping. Samples must be received and processed no more than 7 days after collection. • Please call Client Services at 1-800-305-5198 to order Streck cell-free DNA BCT for your lab.

Assay Range

0.5% - 60%

To establish a clinical cutoff for for Viracor's TRAC™ Kidney dd-cfDNA assay, a total of 77 plasma samples collected from kidney transplant recipients were tested by the analytically validated method. The patient samples tested were obtained from a biorepository source. Of the 77 samples tested, 58 were characterized by the specimen provider to have been collected during a period free of acute rejection (AR), while 19 samples were collected during a period of biopsy-proven AR (humoral and/or cellular) or BK virus associated nephropathy. Receiver operator characteristic (ROC) curve analysis was performed on the results, and demonstrated an area under the curve value of 0.853. Using the ROC results, a cutoff was selected to optimally balance performance parameters. For a cutoff value of 0.69%, the assay sensitivity, specificity, positive predictive value and negative predictive value were 57.9%, 84.5%, 55%, and 86%, respectively.

Method

The Viracor TRAC™ Kidney dd-cfDNA assay determines the percentage of circulating cell-free DNA (cfDNA) in transplant recipients derived from donor grafts. cfDNA is extracted from plasma isolated from whole blood collected in Streck BCT tubes within seven days of collection and unbiased sequencing is performed. NGS and genome-wide recipient genotype data are then analyzed by a bioinformatics pipeline that calculates the percentage of dd-cfDNA present. This test was developed and its performance characteristics determined by Viracor Eurofins. This test has not been cleared or approved for diagnostic use by the U.S. Food and Drug Administration.

This test is not suitable for use during pregnancy, if the donor and recipient are identical twins, if the patient has received multiple transplants from different donors, or if the donor and recipient are siblings from a consanguineous marriage. In these scenarios, the bioinformatics pipeline will generate an inaccurate result.

Related Tests

The following may be appropriate for some patients.

Test Code	Test Name
9000	ImmuKnow®
403066	T Cell Fx - Complete
30360	CMV T Cell Immunity Panel
30929	TruGraf® Blood Gene Expression Test

References

Bromberg JS, Brennan DC, et. al. Biological Variation of Donor-Derived Cell-Free DNA in Renal Transplant Recipients: Clinical Implications. Journal of Applied Laboratory Medicine (2017, September); 2:02, 1-13.

Gielis EM, Ledeganck KJ, De Winter BY, et. al. Cell-Free DNA: An Upcoming Biomarker in Transplantation. American Journal of Transplantation (2015); 15: 2541-2551.

De Vlaminick I, Martin L, Kertesz M, et. al. Noninvasive monitoring of infection and rejection after lung transplantation. Proceedings of the National Academy of Sciences (2015, October 27); 112:43, 13336-13341.

Grskovic M, Hiller DJ, Eubank LA, et. al. Validation of a Clinical-Grade Assay to Measure Donor-Derived Cell-Free DNA in Solid Organ Transplant Recipients. The Journal of Molecular Diagnostics (2016, November); 18:6, 890-902.

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