Viracor | Eurofins Clinical Diagnostics

TRUGRAF®
Powered by Transplant Genomics

TEST CODE: 30929

CPT CODE: 81479

CATEGORY
Transplant

The Only Non-Invasive Test to Rule out Silent Kidney Rejection

Clinical Utility

TruGraf® Blood Gene Expression Test for kidney transplant patients can help providers monitor and identify subclinical rejection in kidney transplant recipients with stable renal function as an alternative to surveillance biopsies in facilities that utilize surveillance biopsies.

About Kidney Transplantation

Kidney transplantation is the optimal treatment for many patients with end-stage renal disease. In 2018, there were 21,167 kidney transplants performed in the U.S.[1] With the development of newer immunosuppressive drugs, more effective anti-microbial prophylaxis, and improved surgical techniques outcomes of kidney transplantation have improved in the past few decades as a result of; however, rejection is s still a problem over time. Routine post-transplant monitoring consists of the measurement of serum creatinine (SCr) and immunosuppressive drug levels. Both are insensitive and non-specific markers of graft damage. As a consequence, in spite of improved short term outcomes, 10 years after transplantation roughly half of transplanted kidneys are no longer still functioning.[2]

A key problem underpinning long term graft loss relates to immune rejection of the grafted kidney, which is mitigated in part by immunosuppressive drug therapy to prevent the recipient's immune system from rejecting the kidney.[3] However, immunosuppressive drugs themselves are associated with significant side effects including the development of opportunistic infections, increased risk of certain cancers, and even direct nephrotoxicity.[3] As such, the management of a transplant recipient involves achieving the right balance between adequate immunosuppression to minimize rejection while avoiding too much immunosuppression, increasing the risk of side effects.

There are significant challenges to detecting injury early when the kidney has the greatest chance of regaining normal function. Approaches to monitoring and detecting kidney injury include intermittent measurements of serum creatinine levels[4,5], immunosuppressive drug levels[4,5] and performing surveillance graft biopsies at some transplant centers.[6,7] Additionally, research suggests that early treatment of subclinical rejection using surveillance biopsies leads to better graft outcomes.[8] However, biopsies are invasive and themselves associated with infrequent but significant risks.[9] Additionally, at present biopsies are evaluated using the Banff criteria, which rely on visual interpretation by a pathologist, and have significant intra-observer variation in interpretation of biopsy results.[10]

Given that surveillance biopsies are an accepted method to look for graft rejection, a clearly treatable cause of graft injury, within the current accepted management approaches for post-renal transplant care, and biopsies are invasive and associated with risk, there is potential clinical utility for non-invasive testing that can identify graft rejection and spare a patient a biopsy. Additionally, transplant clinicians have expressed agreement that such a test could be used in the framework of existing protocols.[11]

The TruGraf test should be used beginning 90 days post kidney transplant on patients who are a recipient of a primary of subsequent deceased or living donor who are at least 18 years of age. The patients should also have a stable serum creatinine (current serum creatinine <2.3 mg/dl, <20% increase compared to the average of the previous three serum creatinine levels).

TruGraf has not yet been studied sufficiently in the following patient populations, including recipients of a combined organ transplantation with an extra-renal organ and/or islet cell transplant, of previous non-renal solid organ and/or islet cell transplantation, those infected with HIV, patients with BK nephropathy, or patients that have nephrotic proteinuria (urine protein >3 gm/day).

Turnaround Time

7 business days from receipt of specimen.

Viracor | Eurofins Clinical Diagnostics

TRUGRAF®

Powered by Transplant Genomics

Specimen Requirements

This test requires special tubes for collection.

- 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.
- A **TruGraf Test Requisition Form** must accompany each specimen. Call Client Services to set up your account, 800.305.5198.
- **Ship specimens FedEx Priority Overnight® to:**
  Transplant Genomics Inc., 46774 Lakeview Blvd., Fremont, CA 94538
- CAUSES FOR REJECTION: Specimens beyond their acceptable length of time from collection as listed in the specimen instructions, or specimen types or containers other than those listed.

Specimen Type	Volume	TruGraf Special Instructions
Whole Blood	**2 PAXgene Blood RNA Tubes**	• Collect (2) whole blood in a PAXgene Blood RNA Tube. Tube must be completely full to maintain proper ratio of blood to anticoagulant. During blood collection, the tube must remain upright and vertically, held below the patient's arm. Allow at least 10 seconds for blood collection and ensure blood has stopped flowing prior to removing from the collection device. • Regarding order of draw: If the PAXgene Blood RNA Tube is the only tube to be drawn, a small amount of blood should be drawn into a "Discard Tube" prior to drawing blood into the PAXgene Blood RNA Tube. Otherwise, the PAXgene Blood RNA Tube should be the last tube drawn in the phlebotomy procedure. • For best results, a 21G or 22G needle is advised. Slower fill times may be observed when using a smaller gauge needle. • After venipuncture, it is critical to mix tubes thoroughly by gently inverting the tube 8-10 times end-over-end immediately after collection. • PAXgene Blood RNA tubes are stable at room temperature for up to 72 hours, at refrigerated temperature for up to 5 days, or frozen >5 days. • Ship samples Monday-Friday. Friday shipments must be labeled for Saturday Delivery. • Can be shipped ambient for next day arrival Monday-Friday, when received within 48 hours of collection. • If shipping refrigerated, samples must be received within 5 days; if shipping frozen and samples should be frozen within 5 days and shipped on dry ice. • Please call 1-844-TRUGRAF for questions regarding specimen instructions or testing.

Assay Range

Qualitative. Reported as: TX (Transplant eXcellence) or not-TX

In validation studies comparing biomarker signatures in blood with histological phenotypes, the sample profile is either correlated or NOT correlated with a phenotype of Transplant eXcellence. TX is defined as serum creatinine <= 2.3mg/dL and stable renal function (<20% variability in current serum creatinine compared to the average over the past 3 measurements), and a biopsy that shows no rejection or no other histological abnormalities.

Method

The TruGraf test is a minimally-invasive test that measures differentially expressed genes in the blood of renal transplant recipients to identify patients who are likely to be adequately immunosuppressed. TruGraf uses DNA microarray technology to determine whether a patient's blood gene expression profile is more similar to that obtained from a reference population classified by simultaneous histological analysis of a biopsy as TX, and likely adequately immunosuppressed, or not-TX, and likely to be inadequately immunosuppressed. The TruGraf test was developed and its performance characteristics determined by Transplant Genomics Inc. This test has not been cleared or approved for diagnostic use by the U.S. Food and Drug Administration. Testing is performed at Transplant Genomics Inc., 46774 Lakeview Blvd., Fremont, CA 94538.

Related Tests

The following may be appropriate for some patients.

Test Code	Test Name
30876	Viracor TRAC™ Kidney dd-cfDNA
9000	ImmuKnow®
30360	CMV T Cell Immunity Panel

The CPT codes provided are based on Viracor Eurofins' interpretation of the American Medical Association's Current Procedural Terminology (CPT) codes and are provided for informational purposes only. CPT coding is the sole responsibility of the billing party. Questions regarding coding should be addressed to your local Medicare carrier. Viracor Eurofins assumes no responsibility for billing errors due to reliance on the CPT codes illustrated in this material.

References

1. Organ Procurement and Transplantation Network. National Data. 2019; https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/# (https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/). Accessed 2/5/2019, 2019.
2. Hart A, Smith JM, Skeans MA, et al. OPTN/SRTR 2014 annual data report: kidney. Am J Transplant. 2016;16(S2):11-46.
3. Halloran PF. Immunosuppressive drugs for kidney transplantation. New England Journal of Medicine. 2004;351(26):2715-29.
4. Kasiske BL, Zeier MG, Chapman JR, et al. KDIGO clinical practice guideline for the care of kidney transplant recipients: a summary. 2010;77(4):299-311.
5. Kasiske BL, Vazquez MA, Harmon WE, et al. Recommendations for the outpatient surveillance of renal transplant recipients. 2000;11(suppl 1):S1-S86.
6. Nankivell BJ, Chapman JR. The Significance of Subclinical Rejection and the Value of Protocol Biopsies. 2006;6(9):2006-12.
7. Henderson L, Nankivell B, Chapman* JJAJoT. Surveillance protocol kidney transplant biopsies: their evolving role in clinical practice. 2011;11(8):1570-5.
8. Rush D, Nickerson P, Gough J, et al. Beneficial effects of treatment of early subclinical rejection: a randomized study. 1998;9(11):2129-34.
9. Schwarz A, Gwinner W, Hiss M, Radermacher J, Mengel M, Haller HJAjot. Safety and adequacy of renal transplant protocol biopsies. 2005;5(8):1992-6.
10. Mengel M, Sis B, Halloran PJAJoT. SWOT analysis of Banff: strengths, weaknesses, opportunities and threats of the international Banff consensus process and classification system for renal allograft pathology. 2007;7(10):2221-6.
11. First MR, Pierry D, McNulty M, et al. Analytical and Clinical Validation of a Molecular Diagnostic Signature in Kidney Transplant Recipients Journal of Transplantation Technologies & Research 2017;7(3):176.
12. First MR, Peddi VR, Mannon R, et al. Investigator Assessment of the Utility of the TruGraf Molecular Diagnostic Test in Clinical Practice. Transplantation Proceedings, 2019, 51, 729-33. https://doi.org/10.1016/j.transproceed.2018.10.024.
13. Friedwald JJ, et al., Development and clinical validity of a novel blood-based molecular biomarker for subclinical acute rejection following kidney transplant. American Journal of Transplantation 2019, 98-109.
14. Marsh C, Kurian SM, Rice J, et al. Application of TruGraf® v1: A Novel Molecular Biomarker for Managing Kidney Transplant Recipients with Stable Renal Function. Transplantation Proceedings. 2019;Epub ahead of print.
15. Proposed Local Coverage Determination MolDX: TruGraf Blood Gene Expression Test (DL38039). Accessed 28 March, 2019 from cms.gov.

MM 1004 REV0 1119

Viracor Eurofins • 1001 NW Technology Drive • Lee's Summit, MO 64086 • Ph 800.305.5198 • Fax 816.347.0143 • Viracor-Eurofins.com