

Transplant assessment

# Now quantify the risk A cfDNA background check every time

CASE STUDIES

### How quantifying background cell-free DNA enables even greater precision with Prospera for rejection assessment

As the experts in cell-free DNA (cfDNA) testing, Natera has refined our workflow based on findings from two million cfDNA tests to now include a first-in-class technique capable of quantifying background cfDNA in a streamlined manner.

When assessing rejection via the Prospera™ transplant assessment test, this pioneering enhancement provides additional information, which may enable an even more precise and confident assessment-particularly in flagging patients at-risk of false-negative interpretations.

# Even more precise, holistic assessment with background cfDNA

#### PATIENT 1



# **Meet Kirk** End-stage renal disease (ESRD)

Transplant in mid-2018

#### THE JOURNEY

Transplant surgery	Post-transplant		
0	6 months	7 months	14 months
Mid 2018	Elevated creatinine levels, indicating acute T cell-mediated rejection (TCMR)	Tested positive for BK viremia, which was immediately treated and resolved	Admitted for herpetic and cytomegalovirus (CMV) esophagitis and was treated with intravenous ganciclovir

#### CLINICAL ASSESSMENT WITH PROSPERA

The Prospera result revealed a low donor-derived cell-free DNA (dd-cfDNA) fraction at 0.38%, indicating a decreased risk for active rejection.

Further Prospera analysis quantified background cfDNA, revealing a level 21x the median - and thereby flagging an increased risk of a false-negative interpretation.

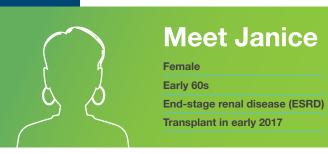
Based on Prospera's enhanced reporting, percutaneous kidney transplant biopsy was performed; the result **confirmed chronic** cellular rejection (via Banff criteria).

#### THE TAKEAWAY

Viral infections can cause an atypical increase in recipient background cfDNA. This inflation may lead to an artificially deflated percentage of dd-cfDNA.

Prospera's novel ability to quantify background cfDNA highlighted an increased risk for a false-negative interpretation.

#### PATIENT 2





#### CLINICAL ASSESSMENT WITH PROSPERA

Prospera result showed a **dd-cfDNA of 0.28%**, potentially a decreased risk for active rejection.

The report also flagged atypical background cfDNA levels that were elevated at ~7x the median.

The resulting percutaneous kidney transplant biopsy revealed BK virus-associated nephropathy and T cell-mediated rejection.

#### THE TAKEAWAY

**BK virus-associated active injury** may contribute to atypical background cfDNA levels.

Prospera's latest enhancement allows for physicians to more effectively identify active rejection that would have otherwise been missed.

#### PATIENT 3

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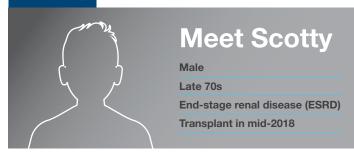
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0	1 month	6 months		
ate 2019 om an nrelated, <i>r</i> ing donor	Diagnosed with dengue fever, followed by acute allograft dysfunction	A biopsy was performed revealing active antibody- mediated rejection. He was then treated with plasmapheresis and intravenous immunoglobulin with clinical resolution		

#### CLINICAL ASSESSMENT WITH PROSPERA

At 7 months post-transplant, he received a Prospera result of 0.16% dd-cfDNA level, indicative of a decreased risk for active rejection.

The Prospera result also revealed a heightened level of background cfDNA at ~13X the median.

A biopsy thereafter showed resolution of ABMR and borderline acute cellular rejection.

#### THE TAKEAWAY

For the first time, further evaluation of background cfDNA levels enabled the physician to identify signs of borderline acute cellular rejection.

This additional information by Prospera can provide a more complete clinical assessment of your transplant patient.

PATIENT 4



### **Meet Sharon**

End-stage renal disease (ESRD) secondary to PKD

#### THE JOURNEY

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Transplant Post-transplant

Late 2018 from a

donor

Presented with four days of worsening deceased diffuse muscle pain

## 1 week

Progressed to a temperature of 101°F (asymptomatic previously). Visited her local

#### 11 months 11 months, 11 months, 1.5 weeks ۲

Tested positive for COVID-19 and intubated at her transplant center. Renal function deteriorated. immunosuppression emergency room was closely managed

#### CLINICAL ASSESSMENT WITH PROSPERA

Prospera was used to assess rejection status on the 20th day of her hospital stay.

The Prospera result showed 0.07% dd-cfDNA with a heightened level of background cfDNA at ~57X the median.

A second Prospera test was drawn on the 25th day of her hospital stay with a result of 0.25% dd-cfDNA and a decreased level of background cfDNA at ~15x the median.

#### THE TAKEAWAY

**COVID-19 may cause very elevated** background cfDNA. Therefore, patients are at-risk for a false negative interpretation, especially when immunosuppression is reduced in response to the infection.

By reporting high background level, Natera proactively alerts the physician if the result may yield a false negative in a high-risk patient.



Powered by highly optimized, proprietary cfDNA technology, Prospera enables you to:



**Catch all rejection types in a single blood draw:** Prospera's unique ability to identify T cell-mediated rejection (TCMR) gives a more holistic view of your patient's rejection status.<sup>1</sup>



Minimize risk of missing active rejection: Prospera is three times less likely to miss an active rejection\*\* than the first-generation donor-derived cell-free DNA test (Negative Predictive Value of 95% vs 84%).<sup>1,2</sup>



**More accurately classify active rejection:** Prospera demonstrated better performance than the first-generation dd-cfDNA test (sensitivity of 89% vs 59%) to identify patients with active rejection.<sup>1,2</sup>

#### References

\*\* 25% prevalence of active rejection

1 Sigdel TK, Archila FA, Constantin T, et al. Optimizing detection of kidney transplant injury by assessment of donor-derived cell-free DNA via massively multiplex PCR. J Clin Med. 2019;8(1):19. 2 Bloom RD, Bromberg JS, Poggio ED, et al. Cell-free DNA and active rejection in kidney allografts. J Am Soc Nephrol. 2017;28(7):2221-2232. doi: 10.1681/ASN.2016091034.

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The test described has been developed and its performance characteristics determined by the CLIA-certified laboratory performing the test. The test has not been cleared or approved by the US Food and Drug Administration (FDA). Although FDA has generally not enforced the premarket review and other FDA legal requirements for laboratory-developed tests in the US, certification of the laboratory is required under CLIA to ensure the quality and validity of the tests. CAP accredited, ISO 13485, and CLIA certified. © 2020 Natera, Inc. All Rights Reserved. PRO\_BR\_CommNeph\_20200416\_NAT-8020141



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