SZABO SCANDIC

Part of Europa Biosite

Produktinformation

- Forschungsprodukte & Biochemikalien
- Zellkultur & Verbrauchsmaterial
- Diagnostik & molekulare Diagnostik
- Laborgeräte & Service

Weitere Information auf den folgenden Seiten!
See the following pages for more information!

Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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AlloSeq cfDNA

Risk Assessment of Allograft Rejection by Measuring dd-cfDNA

An innovative NGS-based solution that enables dd-cfDNA blood testing as a kit for laboratory implementation or send out service

Derrick C, kidney transplant recipient

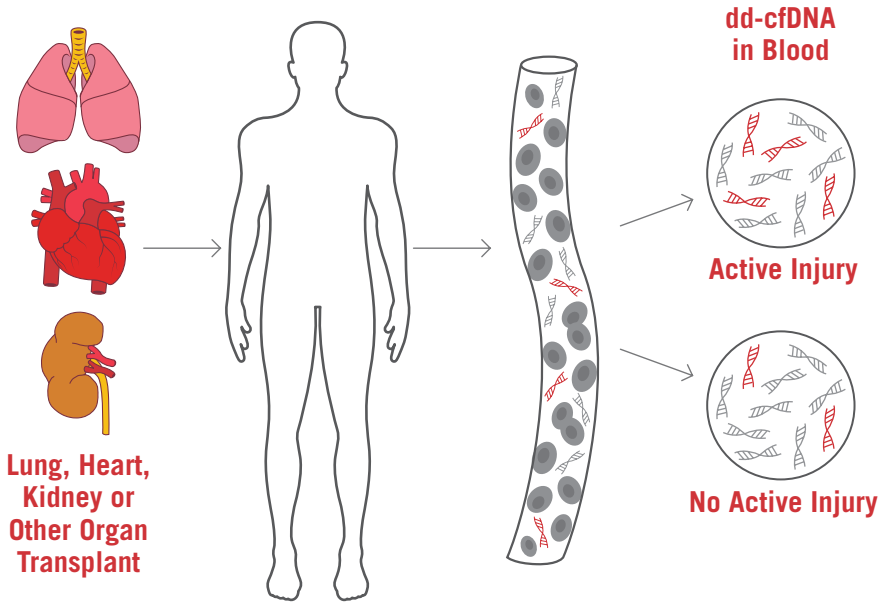
CareDx®

Cell-free DNA: a clear biomarker for organ injury

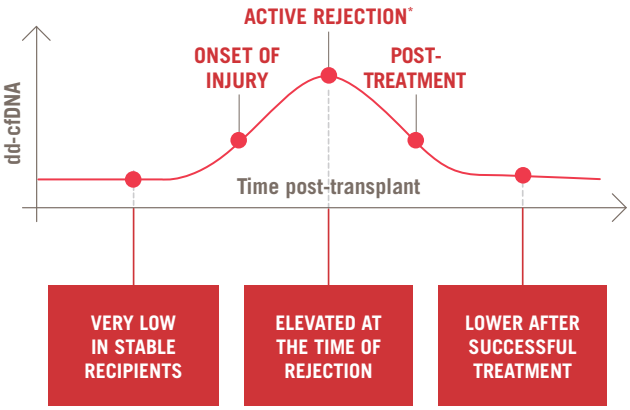
Cell-free (cfDNA) is fragmented DNA in the bloodstream that originates from cells undergoing cell injury and death

When graft injury occurs, donor-derived cell-free DNA (dd-cfDNA) increases in the blood

dd-cfDNA is a powerful, minimally invasive tool for organ transplant surveillance



Allograft surveillance with dd-cfDNA testing: assessment of injury risk



How it is used in action to protocols with ease?

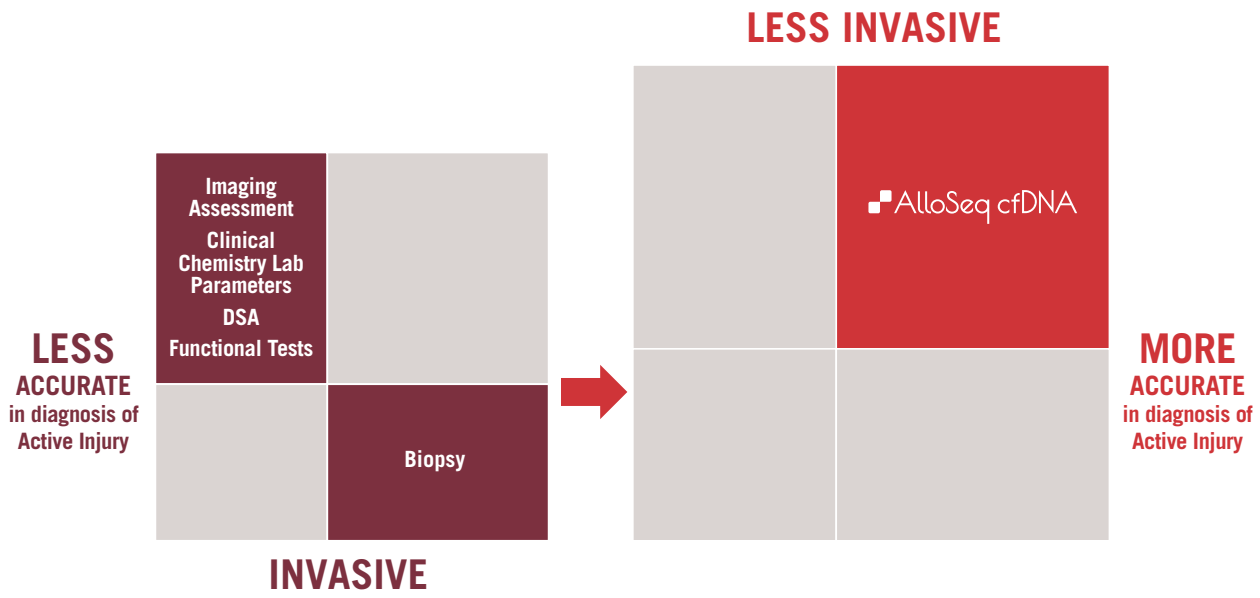
- Injury Surveillance
- For Cause Testing
- Treatment Monitoring
- Immunosuppression Optimization

What is AlloSeq cfDNA?

+ Targets 202 bi-allelic SNPs across 22 autosomes
+ Test up to 24 samples/run
+ Validated on Illumina MiniSeq and MiSeq
+ No prior genotyping required
+ Analytically validated by multi-centric study
+ From cfDNA sample to reported result < 24 hrs with < 1.5 hrs hands-on time
+ Allows reporting dd-cfDNA as fraction
+ Ability to calculate absolute copies
+ Ability to monitor more than one donor cfDNA contributor

dd-cfDNA differentiates between immune quiescence, detection of early graft injury and rejection

+ Minimally invasive
+ More accurate
+ Earlier detection
+ Dynamic biomarker with quantitative approach



AlloSeq cfDNA was developed after the successful clinical validation of AlloSure*

AlloSure is the dd-cfDNA surveillance service that has been clinically and analytically validated for identifying kidney, heart and lung injury.

AlloSure is the most published dd-cfDNA test in transplantation with over 100+ peer reviewed journal publications.

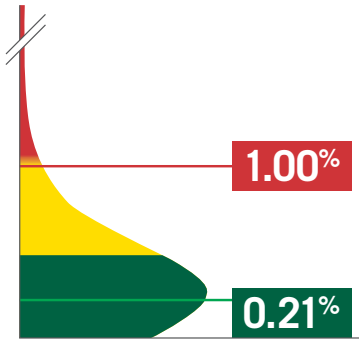
Interpretation of dd-cfDNA results in kidney, heart and lung transplantation

at varying levels provides meaningful, actionable information to your existing clinical setting

Cut-off values suggested are clinically validated by CareDx with service modality AlloSure for assessing the risk of allograft rejection.

KIDNEY

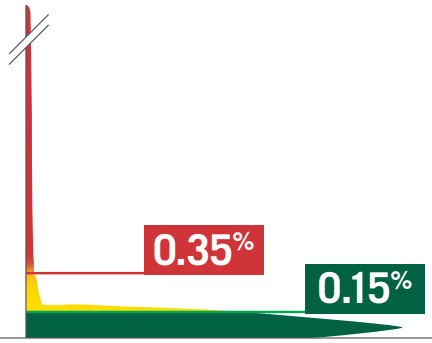
Injury:	1.00%
Elevation:	0.50%
Quiescence:	0.21%



Number of Samples: 68,023

HEART

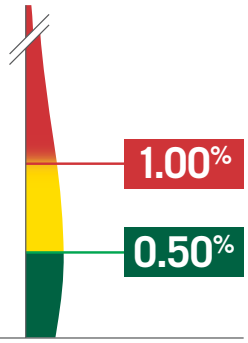
Injury:	0.35%
Elevation:	0.20%
Quiescence:	0.15%



Number of Samples: 13,847

LUNG

Injury:	1.00%
Elevation:	0.85%
Quiescence:	0.50%



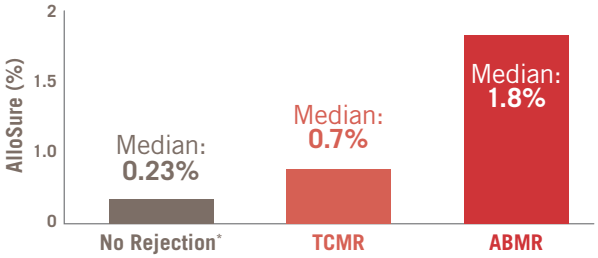
Number of Samples: 673

* AlloSure is available as a dd-cfDNA service within the US only.

AlloSeq cfDNA is based on the clinically validated AlloSure across multiple solid organs with data driven insights from multi-center studies

KIDNEY[1]

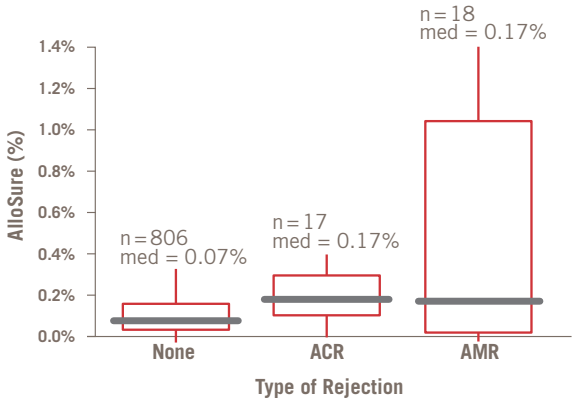
– detects both clinical and subclinical rejection
– differentiates the absence of rejection from TCMR and ABMR



+ AlloSure levels rose a median of 91 days before detection of dnDSA

HEART[2,3]

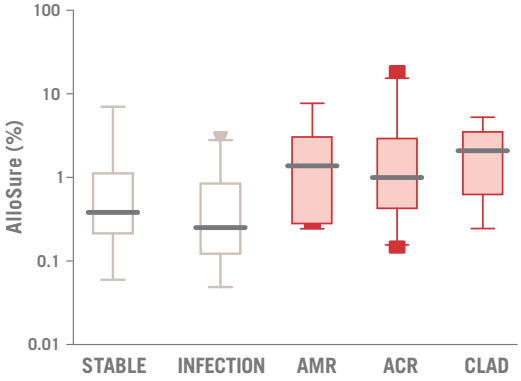
– has been clinically validated to differentiate rejection vs. no rejection.
– was clinically validated in the multi-center prospective D-OAR study



+ ddcfDNA levels are over 2x greater in the rejction groups vs the no rejection group D-OAR
+ No rejection vs. all rejection, p=0.005

LUNG[4,5]

– was clinical validated in a multi-center study
– scores were significantly elevated in allograft rejection & chronic dysfunction



+ AlloSure scores were significantly elevated in the presence of ACR. These findings were further supported by a Stanford study, which observed an elevation in AlloSure results in the event of ACR, AMR, and CLAD

dd-cfDNA surveillance testing can be added to previously established protocols

Months 1, 2 post-transplant

+ Baseline to be established during this time
+ dd-cfDNA is associated with changes immediately post-transplant (ischemia reperfusion injury, or medication dose changes) and may be a potential surrogate marker for these changes
+ Results may contribute to treatment decisions

Months 3, 4 post-transplant

+ dd-cfDNA changes can be used as an associated surrogate marker to monitor the waning of induction immunosuppressants
+ Continue to monitor changes from baseline
+ Maintain continuity in surveillance for patients who transition to the outpatient clinic

Organ	Schedule*	1 Week	1 Month
Kidney	ARTS**	§	Monthly
Heart	HARTS†	§	Monthly
Lung	ALRTS‡	§	Monthly

* All testing should be performed when medically necessary, in accordance with a physician's guidance.

** The Allograft Routine Schedule (ARTS) was clinically validated on the DART study.[6] The KOAR and OKRA registries are assessing the clinical utility of this testing interval.[7] The clinical rational for the ARTS time points was reported by Pai et. al.[8]

† The Heart Allograft Routine Schedule (HARTS) is based on a recommendation from the IMAGE trial.[9] The HARTS was included on OAR and D-OAR registries.[3] The SHORE registry is assessing the clinical utility of this testing interval.[10]

Months 6, 9, 12 post-transplant

+ Monitor for acute rejection
+ Test along with DSA to improve the positive predictive value for antibody mediated Rejection
+ Monitor for changes in dd-cfDNA results that may occur before the development of dnDSA or onset of symptoms

Year 2 Onward: quarterly testing through life of transplant

+ Rejection due to ABMR increases over time and monitoring may provide an early warning of rejection
+ Long-term monitoring of dd-cfDNA levels in lung and heart recipients may add diagnostic aid in the detection of CLAD and CAV, respectively
+ A significant increase in dd-cfDNA may provide early insight into medication non-adherence
+ By identifying patients with dd-cfDNA stable baseline levels immunominimization strategies can be aligned accordingly

2-3 Months	4-6 Months	7-12 Months	12+ Months
Monthly	Every 2 Months	Quarterly	
Monthly			Quarterly
Monthly			Quarterly

‡ AlloSure Lung Routine Schedule (ALRTS) is based on the protocol used for the ALARM-1 Study.[11] The ALAMO study is assessing the clinical utility of this testing interval.[12]

§ Testing using AlloSeq cfDNA assay during the first week and compare results with those obtained at the following time point (first month after transplant) will allow to observe early post-transplant dd-cfDNA kinetics, typically a rapid blood level decay.

In case of clinically suspicion of allograft injury (e.g. abnormal laboratory, abnormal imaging findings, decline in organ function, new DSA), blood for AlloSeq cfDNA is drawn just before biopsy procedure, and if rejection histology findings are reported, dd-cfDNA levels can then be monitored much closely, for example, at week 4 and 8 after initiation of the rejection treatment.

AlloSeq cfDNA – kit or service-based solution

+ NGS based kit - run in your own lab to measure dd-cfDNA without prior genotyping
+ NGS based service* in Stockholm – no lab setup or NGS equipment needed

References

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2. Grskovic M, et al. Validation of a Clinical-Grade Assay to Measure Donor-Derived Cell-Free DNA in Solid Organ Transplant Recipients. *J Mol Diagn.* 2016 Nov;18(6):890-902.
3. Khush KK, et al. Noninvasive detection of graft injury after heart transplant using donor-derived cell-free DNA: A prospective multicenter study. *Am J Transplant.* 2019 Oct;19(10):2889-2899.2019 Oct;19(10):2889-2899.
4. Sayah D, et al. Plasma Donor-derived Cell-free DNA Levels Are Increased During Acute Cellular Rejection After Lung Transplant: Pilot Data. Transplant Direct. 2020 Sep 24;6(10):e608.
5. Khush KK, et al. Donor-derived, cell-free DNA levels by next-generation targeted sequencing are elevated in allograft rejection after lung transplantation. *ERJ Open Res.* 2021 Jan 25;7(1):00462-2020.
6. Bloom RD, et al. Circulating Donor-Derived Cell-Free DNA in Blood for Diagnosing Active Rejection in Kidney Transplant Recipients (DART) Study Investigators. Cell-Free DNA and Active Rejection in Kidney Allografts. *J Am Soc Nephrol.* 2017 Jul;28(7):2221-2232.
7. Evaluation of Patient Outcomes From the Kidney Allograft Outcomes AlloSure Registry (KOAR). ClinicalTrials.gov Identifier: NCT03326076
8. Pai A, et al. Clinical Rationale for a Routine Testing Schedule Using Donor-Derived Cell-Free DNA After Kidney Transplantation. *Ann Transplant.* 2021 Jul 2;26:e932249.
9. Pham MX, et al; IMAGE Study Group. Gene-expression profiling for rejection surveillance after cardiac transplantation. *N Engl J Med.* 2010 May 20;362(20):1890-900.
10. Surveillance HeartCare® Outcomes Registry (SHORE). ClinicalTrials.gov Identifier: NCT03695601
11. Keller M, et al. Donor-derived cell-free DNA as a composite marker of acute lung allograft dysfunction in clinical care. *J Heart Lung Transplant.* 2022 Apr;41(4):458-466.
12. AlloSure Lung Assessment and Metagenomics Outcomes Study (ALAMO). ClinicalTrials.gov Identifier: NCT05050955

AlloSeq cfDNA

The cutting edge solution to detect donor-derived cell-free DNA for transplant surveillance

www.caredx.com/alloseq-cfdna

Want to order AlloSeq cfDNA surveillance tests?

AlloSeq cfDNA Service: Send in samples to CareDx central lab in Stockholm, Sweden, Email: servicetesting@caredx.com or call +46-8-50893900

AlloSeq cfDNA Kit: To learn more about how to bring AlloSeq cfDNA to your own lab, contact your CareDx representative or reach out to us:

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EMEA	orders-se@caredx.com
APAC	orders-aus@caredx.com

Ordering Information

Product	No. RXNs	Product Code
AlloSeq cfDNA - IVD[1]	24	ASCF.1(24)-IVD
AlloSeq cfDNA - RUO[2]	24	ASCF.1(24)
AlloSeq cfDNA Software	N/A	ASCFS1.0
AlloSeq cfDNA Service- RUO only[3]	N/A	N/A

[1]AlloSeq cfDNA is CE-IVD in EU and the UK

[2]In the rest of the world, AlloSeq cfDNA is for Research Use Only. Not to be used for diagnostic procedures. AlloSeq cfDNA is only available outside of the United States.

[3]AlloSeq cfDNA Service is for Research Use Only. Not to be used for diagnostic procedures

*AlloSeq cfDNA Service is Research Use Only

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