InnoGraft

Reinventing graft rejection monitoring

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brochure_RI1001_rev0

Graft rejection remains one of the leading threats to the long-term success of organ transplantation, making effective monitoring critically important

The current gold standard for monitoring, particularly in heart transplantation, is the endomyocardial biopsy (EMB). However, this procedure is invasive, painful, costly, and subject to sampling bias due to its “patchy” nature. Additionally, EMB is typically limited to the first three years post-transplant and is poorly tolerated by pediatric patients.

In other solid organ transplants—such as kidney, liver, and lung—clinicians rely on indirect biochemical markers (e.g., creatinine, ALT/AST, bilirubin, or spirometry), which are non-specific and often reflect late-stage graft injury rather than early immune activity. As a result, these approaches delay diagnosis and hinder the ability to effectively tailor immunosuppressive therapy.

All transplant recipients require lifelong immunosuppressive therapy to prevent graft rejection. Standard regimens typically include calcineurin inhibitors (such as tacrolimus), antimetabolites (like mycophenolate mofetil), and corticosteroids. However, immunosuppression is a delicate balance: overtreatment increases the risk of infections, malignancies, and drug-related toxicity, while undertreatment raises the likelihood of immune-mediated graft injury.

Current monitoring tools are insufficient to fine-tune the delicate balance between over- and under-immunosuppression - particularly during the chronic phase of transplantation, when subtle signs of immune activity often go undetected.

There is a strong, unmet need for continuous, non-invasive, and precise surveillance

Long-term studies have shown that graft rejection can occur many years after transplantation—often silently, until irreversible damage has already taken place.

- In heart transplants, late rejection (beyond 5 years) contributes to 20–30% of chronic graft loss.
- In kidney transplants, antibody-mediated rejection remains the leading cause of graft failure beyond 10 years.
- Liver transplant recipients face ongoing risks of subclinical rejection even a decade post-surgery.

Despite these risks, most patients are no longer monitored beyond the first three years after transplantation.

There is an urgent unmet need for longitudinal, non-invasive surveillance tools that enable clinicians to:

- Detect rejection early and silently
- Dynamically optimize immunosuppressive therapy
- Reduce drug-related toxicity while preserving long-term graft function

InnoGraft: A Paradigm Shift

What it is:

InnoGraft is 4bases' cfDNA platform for longitudinal monitoring of solid-organ transplant recipients. From a single plasma sample, it quantifies donor-derived cell-free DNA (dd-cfDNA), delivering rapid, precise insight into graft integrity—without the risks and costs of biopsy.

How it works:

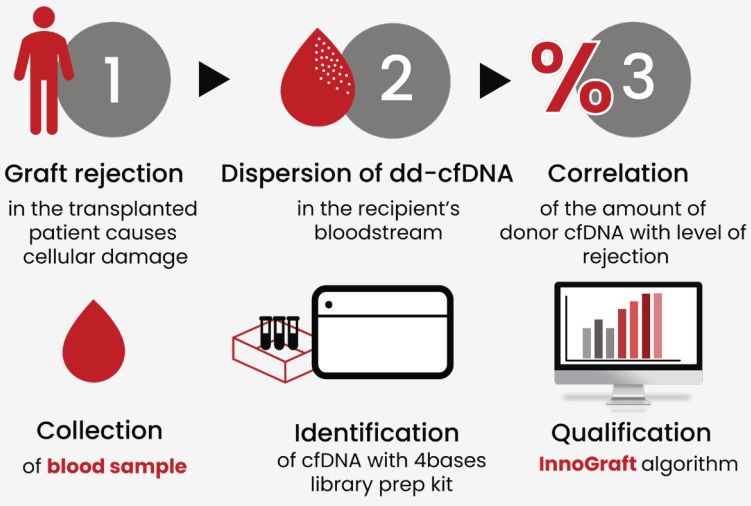
During rejection, injured donor cells release DNA fragments into the recipient's bloodstream. InnoGraft detects and measures this donor-specific cfDNA, providing molecular evidence of immune injury days—or even weeks—before clinical signs or routine chemistry change.

Why it is unique?

Most dd-cfDNA assays either require prior donor genotyping or analyse only a handful of indels. InnoGraft deploys a proprietary panel of **94 highly polymorphic single-nucleotide polymorphisms (SNPs)** that:

- Carry **high minor-allele frequencies** across all major ethnicities
- **Differentiate donor from recipient** without any pre-sequencing of donor DNA
- Generate a **robust signal** even when donor DNA is present at very low levels

THE SCIENTIFIC PRINCIPLE BEHIND INNOGRAFT



This design enables accurate, scalable monitoring for virtually any donor–recipient pair—free of the logistical burden and turnaround delays of donor sequencing.

Core Innovation: cfDNA Discrimination via SNP-Based Allelic Analysis

Following transplantation, a patient's bloodstream contains a mixture of cell-free DNA (cfDNA) originating from both the recipient's own tissues and the donor graft.

The core innovation behind InnoGraft lies in its ability to **deconvolute this mixture** through a sophisticated bioinformatic model trained to recognize **donor-specific allelic patterns.**

By analyzing **allelic frequencies across 94 highly polymorphic SNP loci**, InnoGraft detects subtle shifts that reflect changes in the proportion of donor-derived cfDNA—often signaling early immune-mediated graft injury.

These shifts are interpreted by a **proprietary AI-powered algorithm**, which generates a **quantitative Rejection Index**.

The entire workflow requires only a **peripheral blood draw** and delivers results in under 24 hours, including sequencing and analysis—enabling clinicians to act quickly and confidently.

HOW INNOGRAFT WORKS

Blood sample collection
Peripheral blood sample collected from transplant recipient

Library preparation with 4bases kit
cfDNA is extracted and amplified using SNP-targeting reagents

NGS sequencing
Fast sequencing on major NGS platforms

AI-driven quantification and report
Algorithm quantifies donor cfDNA% and issues digital report

Key benefits of InnoGraft

- Non-invasive: Requires only a blood sample
- Safe and repeatable: Suitable for pediatric and adult patients
- No need for donor genotyping
- High sensitivity: Detects early-stage immune activity
- Rapid turnaround: Digital report in <24h
- Scalable: Applicable to heart, kidney, liver, and lung transplantation
- Cost-effective: Avoids hospitalization, sedation, and pathology
- No needs for an external lab or sample shipments

Technical Details: Library Preparation, Sequencing and Data Analysis

The InnoGraft assay is built on an **amplicon-based library preparation protocol**, specifically optimized to target a panel of **94 highly polymorphic SNPs** with exceptional reproducibility and sensitivity.
The hands-on processing time is approximately **1 hour**, with a total workflow of around **4 hours** from DNA extraction to completed library and sequencing.
The protocol supports **high-throughput multiplexing**, enabling up to **96 samples** to be processed in a single sequencing run. Each sample requires approximately **1 gigabase (Gb)** of sequencing data (roughly 3 million reads), depending on the sequencing platform used. This level of coverage is sufficient to detect donor-derived cfDNA fractions below 1%, allowing for **early detection of graft injury—before clinical symptoms emerge.**

The workflow is compatible with multiple **NGS platforms**, allowing for **flexible, fast, and decentralized deployment**.

InnoGraft also features a **proprietary, cloud-based data analysis platform**. Users can upload raw FASTQ files directly from the sequencer, which are processed through a **fully automated bioinformatics pipeline**.

The result is a clear, concise **digital report** that quantifies the percentage of donor-derived cfDNA.
Importantly, the platform supports **longitudinal monitoring**: clinicians can track cfDNA trends over time, enabling **personalized immunosuppressive management** and **early intervention** in response to signs of rejection.

Join the InnoGraft Early Access Program

Clinical centers worldwide are invited to be at the forefront of innovation in transplant care by joining our **Early Access Program (EAP)**.

This initiative offers a unique opportunity to:

- **Integrate InnoGraft into your existing monitoring workflows**, enhancing precision and patient care
- **Contribute to the clinical validation of InnoGraft** in heart and other solid organ transplant recipients
- **Explore the impact of cfDNA monitoring on immunosuppressive** therapy modulation, paving the way for more personalized and adaptive treatment strategies

Be among the first to experience how InnoGraft can transform your approach to rejection surveillance—**non-invasive, real-time, and clinically actionable.**

And let's reinvent graft rejection monitoring together!

InnoGraft is currently available as a Research Use Only (RUO) product with international patent protection (including US20210062264A1 and WIPO WO2019149673A1).

Clinical centers worldwide are invited to **join the Early Access Program**.

For more information contact 4bases
at **info@4bases.ch** or visit our website at **www.4bases.ch**.

Product	Cod.	Tests number
InnoGraft	Series RI1001	16 & 96

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