Chimerism monitoring after transplantation is now easier, more sensitive, and more precise

Dvysr®

Improving chimerism measurement in post-transplant patient monitoring

■■■ Hematopoietic cell transplantation (HCT) is the predominant curative treatment for many malignant and non-malignant haematological diseases. Each year, over 50,000 HCTs are performed world-wide. Better pre-transplantation matching methods, treatment and follow-up has led to increased patient survival, with nearly one million patients worldwide today living with donated Hematopoietic cells. Better post-transplant follow-up can further improve the quality of life for these patients, as well as reduce health care costs. Donor engraftment and mixed chimerism must be carefully monitored after transplantation.

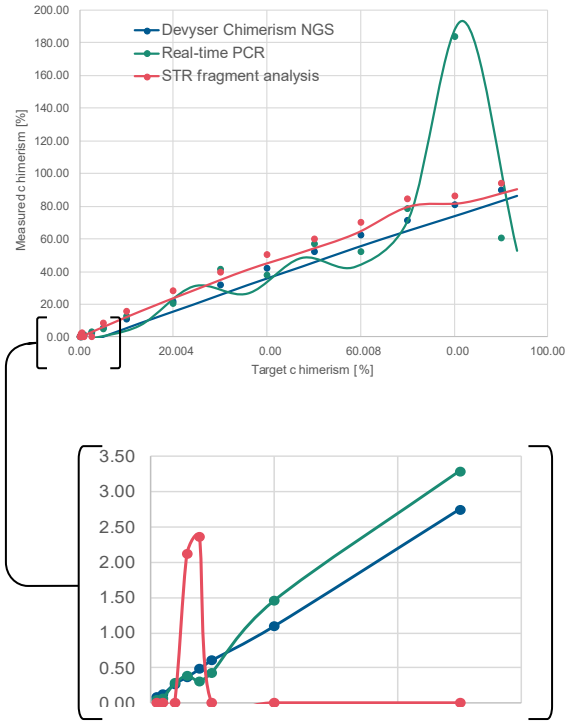
Early detection of graft rejection and disease relapse following HCT improves patient outcomes by allowing treatment to be initiated as quickly as possible after ofset of relapse.

While early detection makes a real difference in post-transplant patient management, the methods commonly used today are associated with challenges.

These include:

- Real-time PCR methods are sensitive but have a low accuracy and precision at elevated levels of mixed chimerism
- STR fragment analysis methods are less sensitive and require frequent monitoring to allow early enough detection of relapse to increase the chances for successful intervention
- A combination of real-time PCR and STR fragment analysis methods enables effective monitoring but takes time and requires multiple protocols
- Data analysis and interpretation can be a challenge, especially when using a combination of test

Devyser Chimerism for NGS



■■■ Devyser Chimerism for NGS is a CE-IVD kit that provides your lab with one simple protocol for fast and reliable chimerism measurement and monitoring in transplanted patients. Complete relapse monitoring is possible with high sensitivity, accurate measurement and a custom software that makes it easy to follow chimerism trends in patients.

Chimerism analysis using NGS enables high sensitivity and accurate measurement throughout the dynamic range. This is achieved by combining the sensitive analysis of real-time PCR with the accurate measurements at high chimerism levels of STR fragment analysis, as illustrated in these two diagrams.

The first diagram shows high accuracy and correlation between Devyser Chimerism for NGS and STR fragment analysis at high chimerism levels (more than >1% of minority fraction). It is also clear that real-time PCR measurements are generally not accurate at chimerism levels above 20% of minority fraction.

The second diagram, a magnified view of the low end of the range, shows that STR fragment analysis has its limitations to correctly measure minority fraction below 3-5%. However, Devyser Chimerism for NGS and real-time PCR show high accuracy and correlation at low level minority fraction.

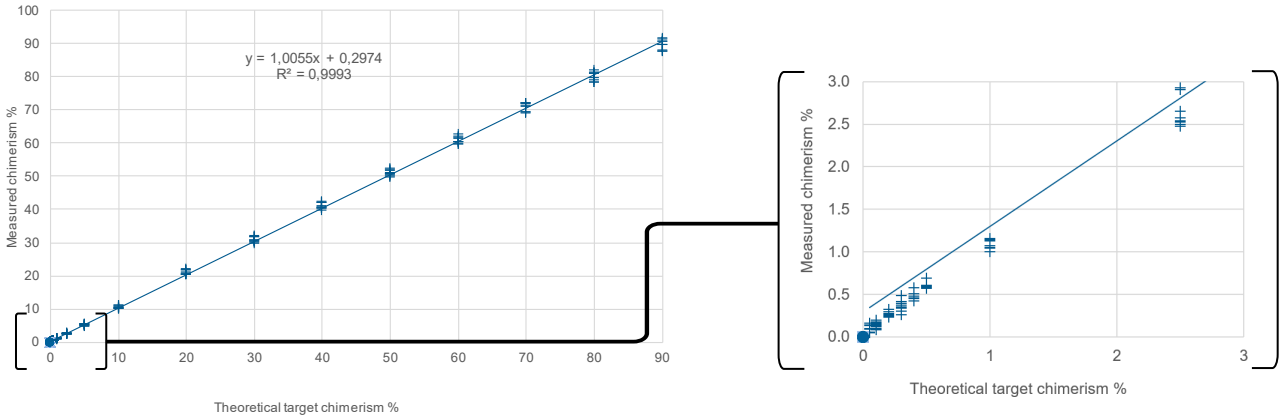
Kit features and advantages

High sensitivity allows very early detection of relapse

■■■ Very early detection of relapse is possible thanks to high sensitivity and accurate measurement down to 0.05% minority fraction chimerism, allowing true monitoring of micro-chimerism.

- Detects down to 0.05% fraction of chimerism
- Accurate and precise measurement over the entire dynamic range from 0.05 - 100% chimerism using a single method

- Allows earlier detection of graft rejection and disease relapse
- One measurement method regardless of the level of mixed chimerism
- Allows true detection and monitoring of micro-chimerism



Kit features and advantages

Fast and effective workflow from patient sample to report

■■■ A complete solution including NGS library preparation and software for data analysis and reporting. A unified workflow from initial screening of recipient/donor pairs to life-long patient monitoring. One tube NGS library prep with just 45 minutes hands-on time.

- A single workflow for both screening and monitoring
- Simple and streamlined workflow with less than 45 minutes hands-on time needed for the complete procedure
- Screening samples are sequenced only once

- Eliminates the need for sample-specific primers and patient-specific marker tracking
- Maximizes flow cell usage and minimizes sequencing costs
- One universal reagent mix for all patients helps reduce reagent wastage and the need for keeping multiple reagents in stock
- Easy to set up, run and maintain

Kit features and advantages

Simple and flexible data analysis

■■■ The ADVYSER software is used for both marker screening and patient monitoring. The software suggests suitable marker pairs for patient monitoring, editable at any time. It allows analysis and visualization of an unlimited number of monitoring samples and cell types to be followed for every patient.

- User-friendly, designed-for-purpose software perfectly complements testing kit
- One easy-to-use software for simplified marker selection and monitoring

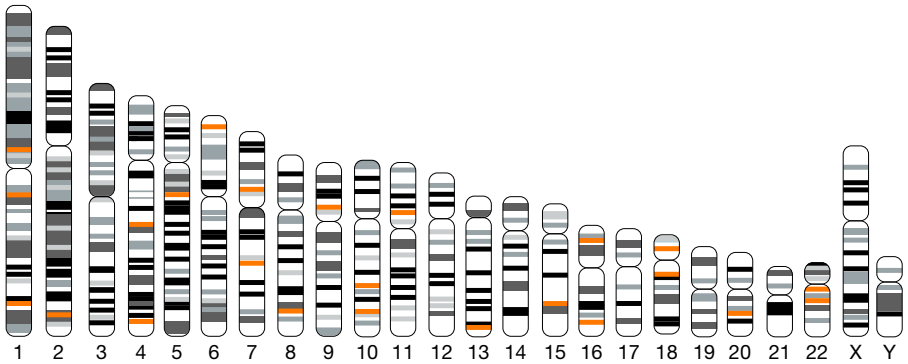
- Eliminates time-consuming, manual and complex results analysis and calculations
- Reduces the risk for potential sample mix-up
- Allows monitoring of dual donors

How this is achieved

24 highly discriminative indel markers

■■■ Screening and monitoring is performed using one reagent mix for all genetic markers. All 24 indel markers have strong discriminative power with low bias from ethnic parameters, and ability to analyse HLA identical siblings. The markers also allow sensitive detection combined with accurate and precise quantification of mixed chimerism.

- Markers were carefully selected using data mining from human genome databases, followed by empirical studies to verify their discriminative power
- Genetic markers with population independent discriminative power distributed across 17 chromosomes

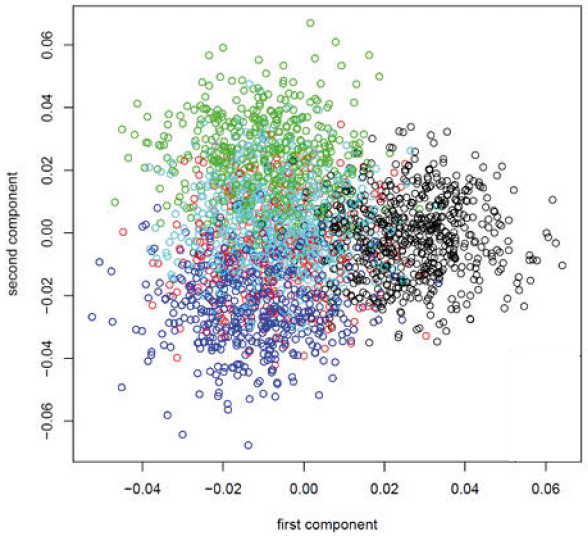


Genetic markers distributed over 17 chromosomes

- Enables efficient screening and monitoring of patients with both matched related and unrelated donors
- Allows highly sensitive detection of low level mixed chimerism as well as accurate and precise quantification throughout the dynamic range (0.05-100%)
- Cost effective: maximizes flow cell usage and minimizes sequencing costs

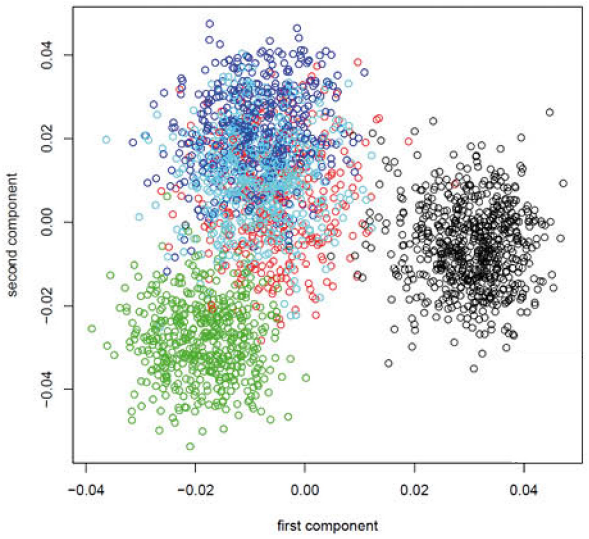
How this is achieved

24 highly discriminative indel markers



PCA for Devyser Chimerism markers:

- These markers are able to distinguish individuals from the same population or family with no population bias
- Low FST-index and LD



PCA for 48 random markers:

- Randomly selected markers capture the variation between populations making it difficult to distinguish individuals from the same population due to population bias
- High FST-index and LD

PCA: Principal Component Analysis

- AFR (African)
- AMR (Admixed American)
- EAS (East Asian)
- EUR (European)
- SAS (South Asian)

How this is achieved

Robust performance with highly variable amounts of input DNA

- The assay can be run with highly variable amounts of input DNA

- Suitable for various sample types, including DNA extracted from whole blood, bone marrow and enriched cell populations
- Obtain high accuracy even with a limited amount of DNA

Expected chimerism: 20%

DNA input	Measured %	CV %
15 ng	20	1.0
7.5 ng	20	0.5
3.75 ng	20	8.5
1.85 ng	18	5.9
0.9 ng	19	6.3

Expected chimerism: 5%

DNA input	Measured %	CV %
15 ng	5	1.0
7.5 ng	5	4.3
3.75 ng	5	1.8
1.85 ng	5	8.5
0.9 ng	3	31.0

Workflow - in short

■■■ One streamlined workflow allows your lab to perform marker screening and patient monitoring in parallel, for multiple samples, in one simple workflow.

Fast and reliable results

- Significantly reduces assay complexity and hands-on time
- Significantly reduces risk of sample contamination

- Less than five hours total assay time
- Minimal hands-on time (<45 minutes) suitable also for processing of a large number of samples

Efficient use of resources

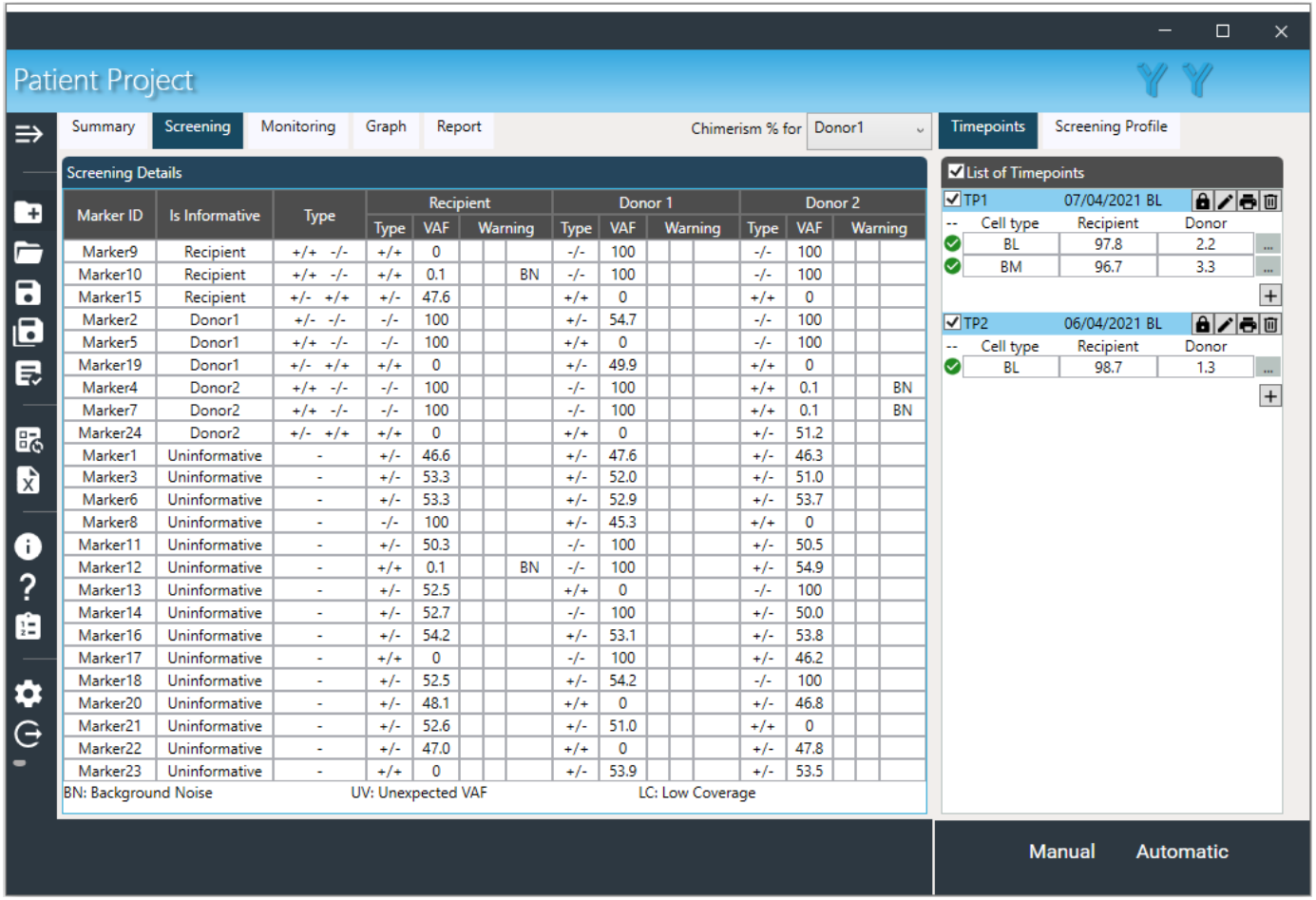
- One-tube solution
- One kit for all patients
- Streamlined, simple and robust NGS workflow uses just one multiplex PCR reaction per patient sample

- Eliminates the need for sample replicates
- Screening samples sequenced only once
- Maximizes flow cell usage and minimizes sequencing costs

Data analysis

Marker screening

- Automatic comparison and identification of up to 24 informative markers in a recipient/donor pair
- Customisable marker selection or approval of the automated selection



Marker ID	Is Informative	Type	Recipient Type	Recipient VAF	Recipient Warning	Donor 1 Type	Donor 1 VAF	Donor 1 Warning	Donor 2 Type	Donor 2 VAF	Donor 2 Warning
Marker9	Recipient	+/+ -/-	+/+	0		-/-	100		-/-	100	
Marker10	Recipient	+/+ -/-	+/+	0.1	BN	-/-	100		-/-	100	
Marker15	Recipient	+/- +/+	+/-	47.6		+/+	0		+/+	0	
Marker2	Donor1	+/- -/-	-/-	100		+/-	54.7		-/-	100	
Marker5	Donor1	+/+ -/-	-/-	100		+/+	0		-/-	100	
Marker19	Donor1	+/- +/+	+/+	0		+/-	49.9		+/+	0	
Marker4	Donor2	+/+ -/-	-/-	100		-/-	100		+/+	0.1	BN
Marker7	Donor2	+/+ -/-	-/-	100		-/-	100		+/+	0.1	BN
Marker24	Donor2	+/- +/+	+/+	0		+/+	0		+/-	51.2	
Marker1	Uninformative	-	+/-	46.6		+/-	47.6		+/-	46.3	
Marker3	Uninformative	-	+/-	53.3		+/-	52.0		+/-	51.0	
Marker6	Uninformative	-	+/-	53.3		+/-	52.9		+/-	53.7	
Marker8	Uninformative	-	-/-	100		+/-	45.3		+/+	0	
Marker11	Uninformative	-	+/-	50.3		-/-	100		+/-	50.5	
Marker12	Uninformative	-	+/+	0.1	BN	-/-	100		+/-	54.9	
Marker13	Uninformative	-	+/-	52.5		+/+	0		-/-	100	
Marker14	Uninformative	-	+/-	52.7		-/-	100		+/-	50.0	
Marker16	Uninformative	-	+/-	54.2		+/-	53.1		+/-	53.8	
Marker17	Uninformative	-	+/+	0		-/-	100		+/-	46.2	
Marker18	Uninformative	-	+/-	52.5		+/-	54.2		-/-	100	
Marker20	Uninformative	-	+/-	48.1		+/+	0		+/-	46.8	
Marker21	Uninformative	-	+/-	52.6		+/-	51.0		+/+	0	
Marker22	Uninformative	-	+/-	47.0		+/+	0		+/-	47.8	
Marker23	Uninformative	-	+/+	0		+/-	53.9		+/-	53.5	

BN: Background Noise UV: Unexpected VAF LC: Low Coverage

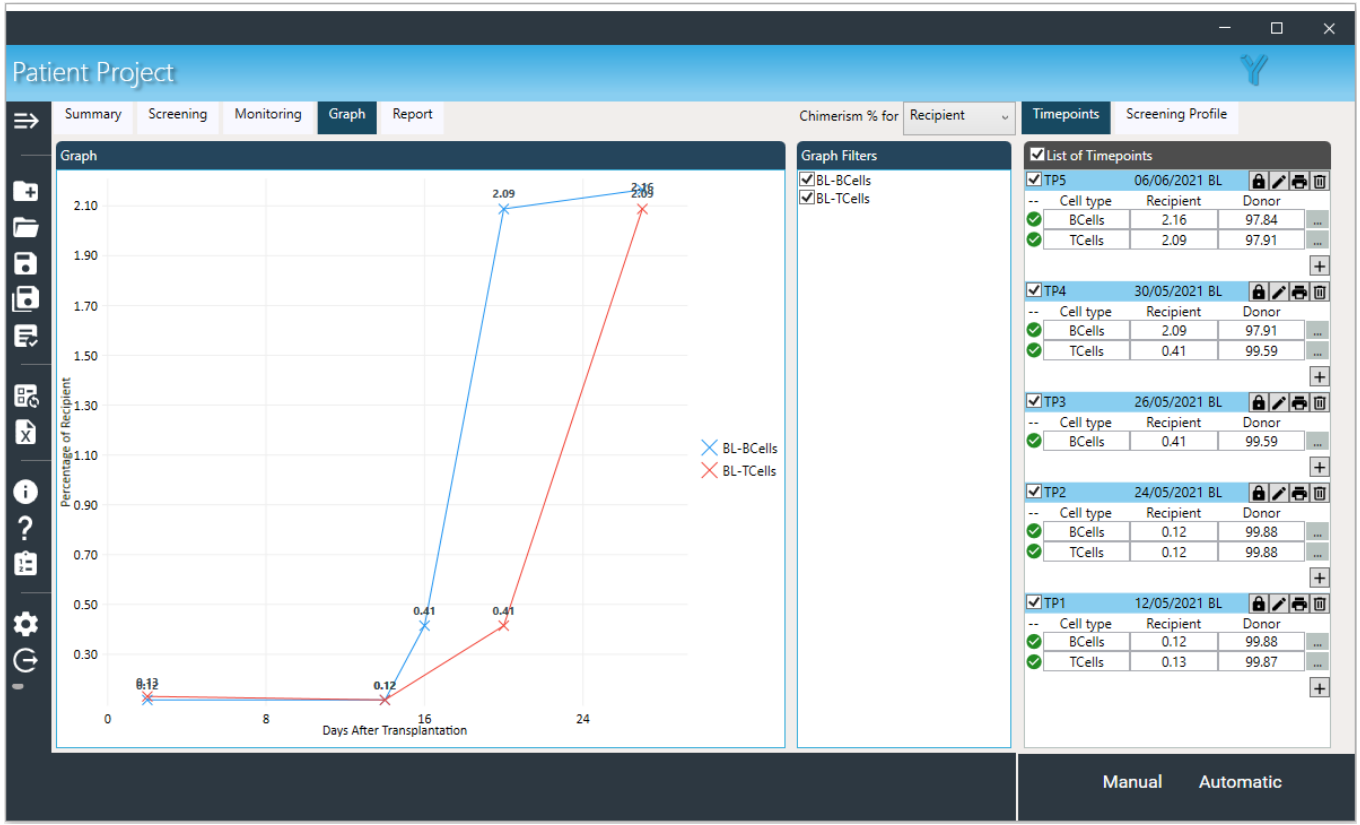
Data analysis

Monitoring

- Automatic calculation of mixed chimerism
- Display of results visualizes patient monitoring over time
- Visualisation can include an unlimited number of cell types for each patient
- Allows monitoring of dual-donors

Reporting

- Generate custom reports
- Export patient data for use in other systems



Short facts - Devyser Chimerism for NGS

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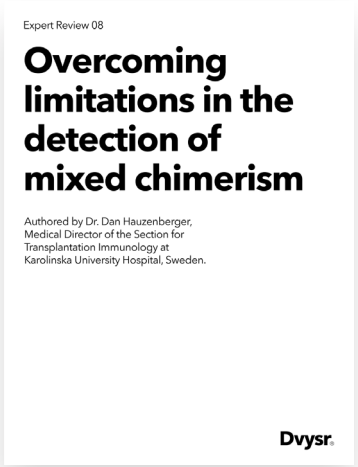
Read more about the product:

bit.ly/more-about-transplantation
bit.ly/more-about-devyser-chimerism
bit.ly/chimerism-knowledge-hub

Discover our Expert Review: Overcoming limitations in the detection of mixed chimerism

bit.ly/chimerism-whitepaper



Article numbers
Devyser Chimerism CE-IVD kit
8-A107

Accessories
Devyser Library Clean
8-A204

Devyser Index Plate A
8-A200

Devyser Index Plate LB-A
8-A202

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