Kihealth

From Years to Weeks

Turning beta cell death into a real-time endpoint.

A first-of-its-kind biomarker quantifying active beta-cell apoptosis **enabling earlier endpoints, improved patient stratification and a more accurate assessment of therapeutic efficacy.**

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Ada Scientific Sessions | 2026

What we'll cover

01 The Measurement Gap In Pediatric Diabetes

02 DELAY Trial Reanalysis Teplizumab PD

03 The science: beta-cell-specific cfDNA methylation

04 Stratification & clinical implications

05 Analytical & clinical validation

06 Future directions + Q&A

We diagnose pediatric T1D after most beta cells are gone.

70–80%

Beta-cell mass already lost

by clinical T1D diagnosis (DiMeglio et al., Lancet 2018)

30–60%

Pediatric T1D diagnosed in DKA

at first clinical presentation (Cherubini et al., 2020)

[X] Years

Trial endpoint timelines

with C-peptide and HbA1c as readouts (Sims et al., Diabetes 2022)

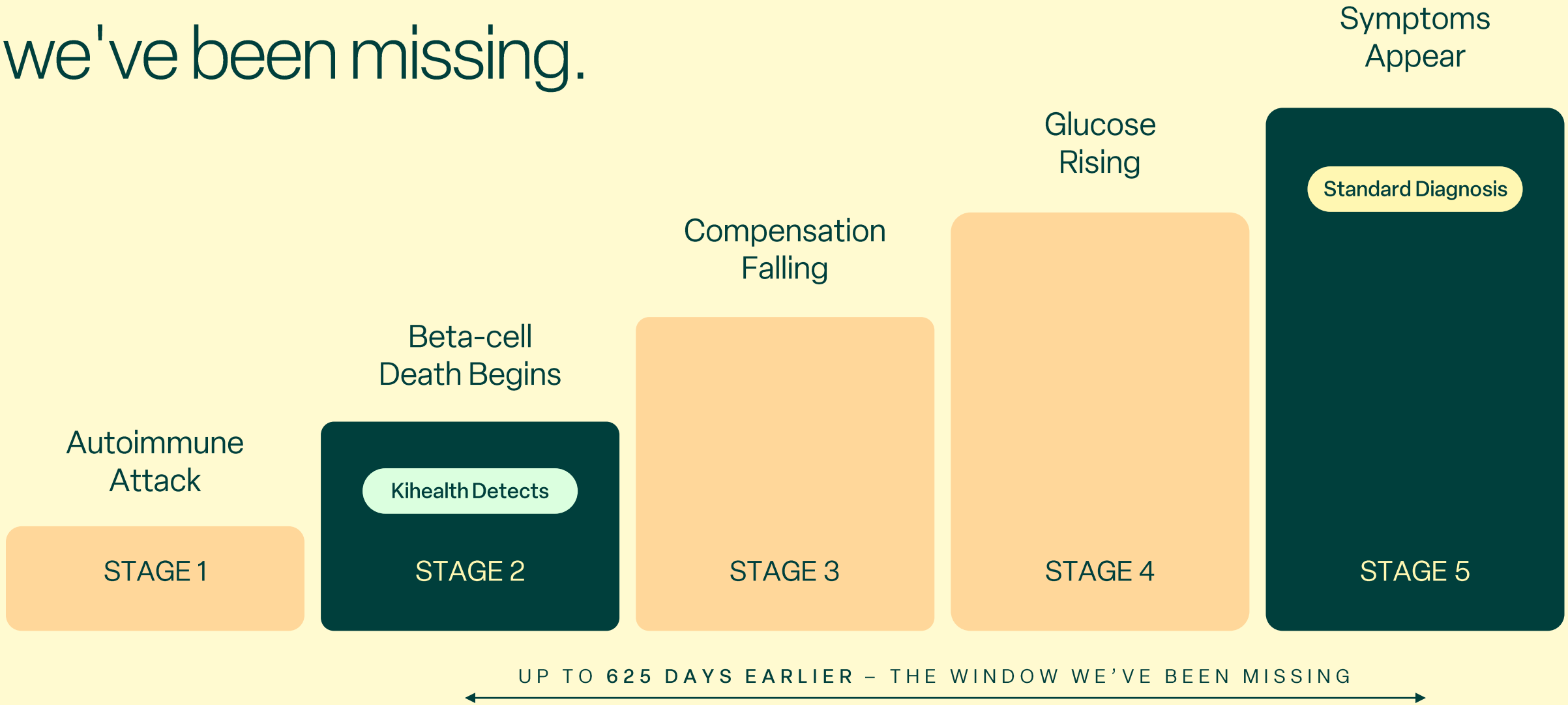
THE MEASUREMENT GAP

Current biomarkers measure downstream consequences.

Biomarker	What it measures	Limitation for active disease
HbA1c	Cumulative glycemic exposure (3 mo)	Reflects historical metabolic state-not current cellular dynamics
Glucose	Acute glycemic state	Rises only after >50% β-cell mass loss
C-peptide	Residual β-cell secretory function	Declines after destruction, measures what's left-not what's being lost
Autoantibodies	Immune autoimmunity (risk)	Identifies who may develop disease-not who is actively progressing

THE MEASUREMENT GAP

The window we've been missing.



THE SCIENCE

Beta cells leave an epigenetic signature when they die.

01

Beta-cell-specific demethylation

The insulin (INS) gene locus is uniquely demethylated in pancreatic β-cells. No other tissue maintains this methylation pattern.

02

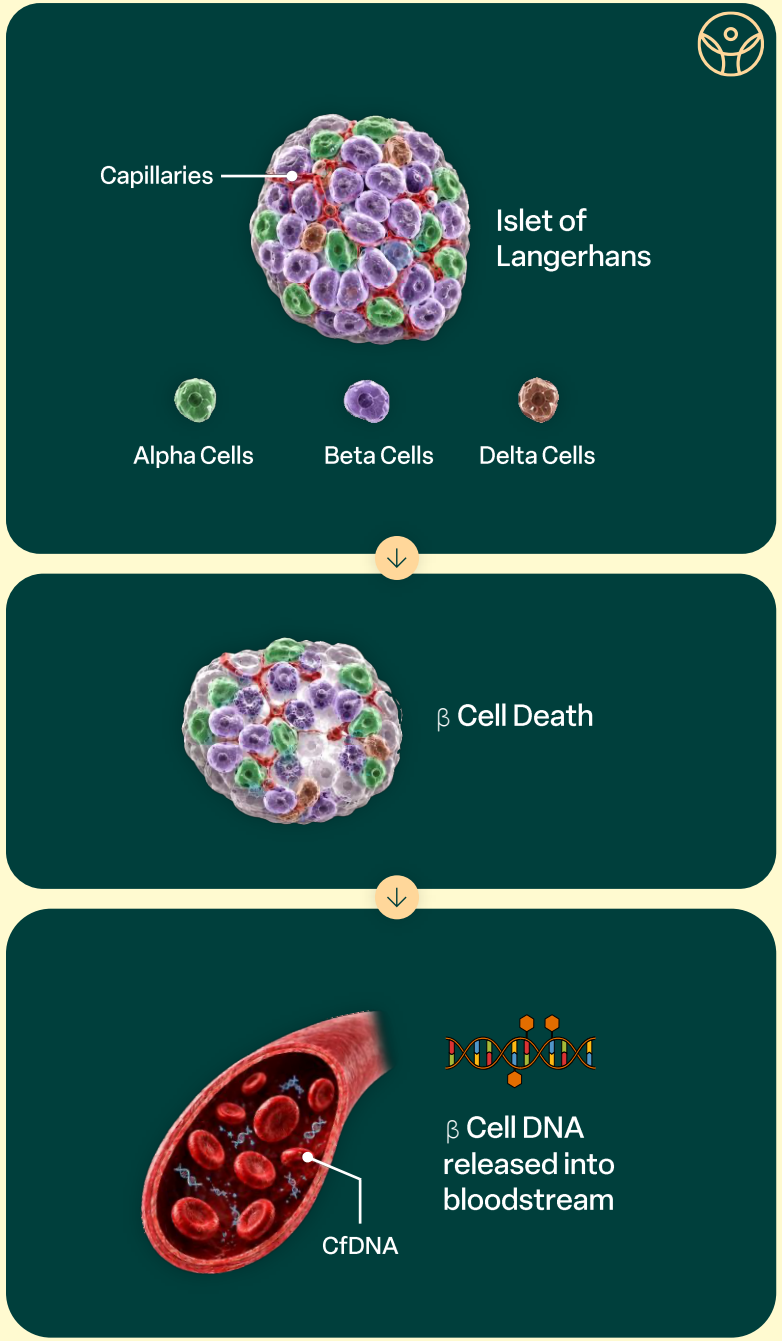
Release during apoptosis

When β-cells die, cell-free DNA (cfDNA) fragments -including the demethylated INS locus-enter circulation within minutes.

03

Detectable in plasma

A standard venous blood draw captures the demethylated INS cfDNA signal - a direct readout of β-cell turnover in vivo.



Akirav et al., PNAS 2011 · Husseiny et al., Diabetes 2014 · Lebastchi et al., Diabetes 2013 · Herold et al., Diabetes 2012

THE SCIENCE

Multiplex ddPCR across three INS CpG regions.

Plasma cfDNA

Automated low-abundance extraction Norgen tubes (5-day stability)

HpaII digestion

Parallel methylation-sensitive + mock-treated reactions per sample

Multiplex ddPCR

INS −233, INS −135, INS +399 Bio-Rad QX200 platform

Poisson quantification

Absolute % unmethylated INS Multi-site signal corroboration

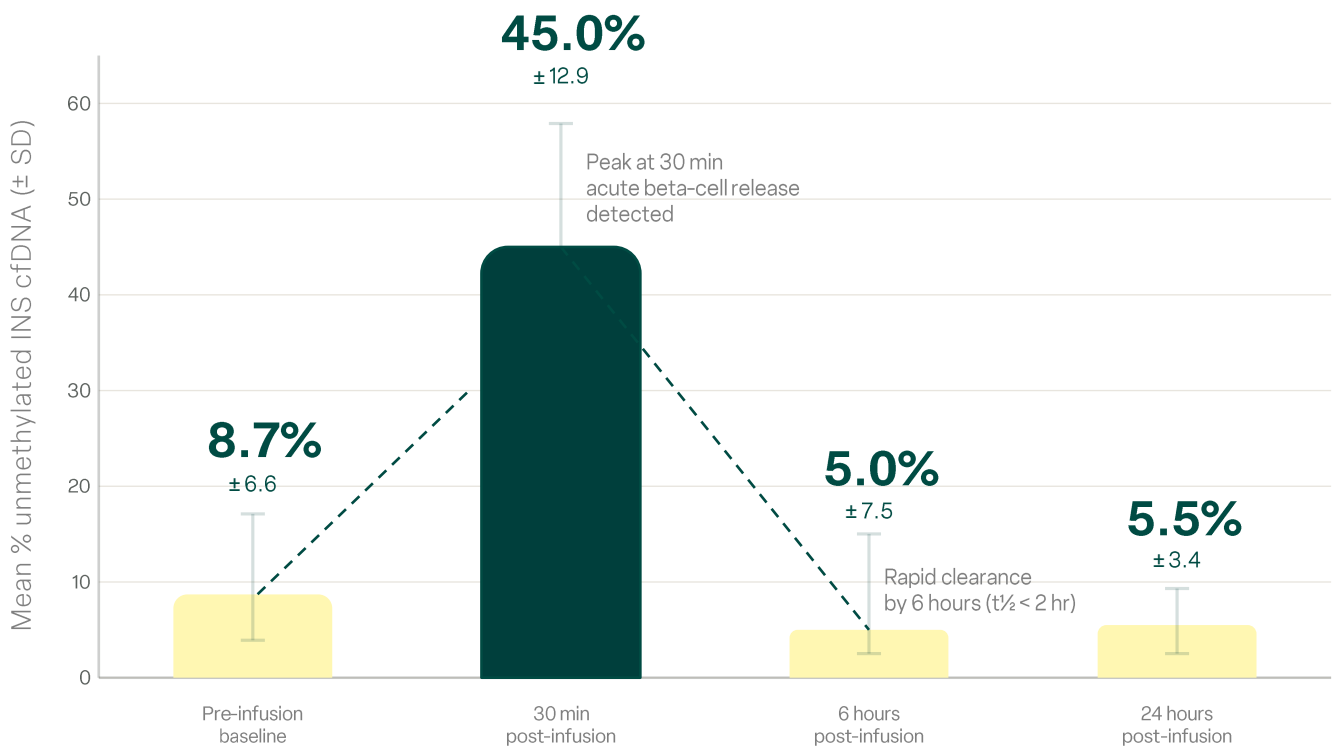
Multi-site design

Interrogating three INS CpG regions improves confidence in beta-cell-origin signal detection and reduces dependence on any single locus — corroborated by BLAST chromosome 11-restricted alignment + HpaII site confirmation.

Empirical proof: islet infusion kinetics.

Serial samples from beta-cell/islet infusion recipients — provided by Dr. Herold (Yale).

Islet Infusion Kinetics — Empirical Real-Time Signal
Beta-cell-derived cfDNA peaks at 30 min, clears by 6 hours



Key Implications

Acute peak captured

5× rise from baseline (8.7% → 45.0%) detected within 30 min of beta-cell release event.

Rapid plasma clearance

Signal returns to baseline by 6 hours (5.0%) — consistent with ~2 hr cfDNA half-life (Lo et al., 2010).

Real-time, not cumulative

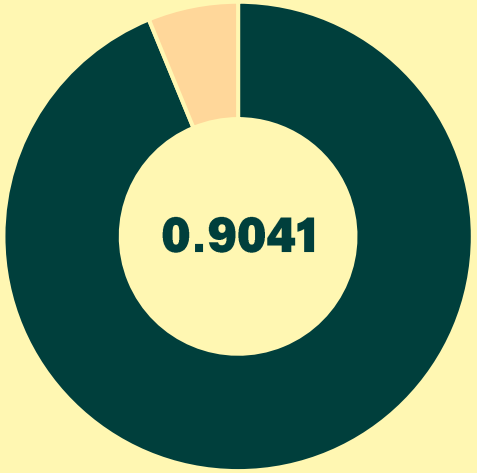
A single draw reflects β-cell death within the prior hours — not historical damage.

Non-redundant with C-peptide

C-peptide measures residual function; this assay measures active rate of cell death.

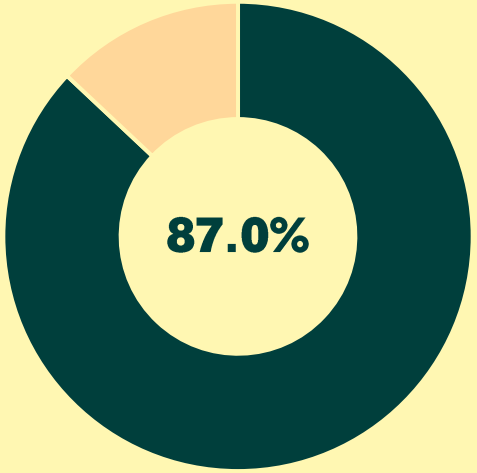
Analytical performance.

Per CLIA high-complexity laboratory standards. Full validation package on file.



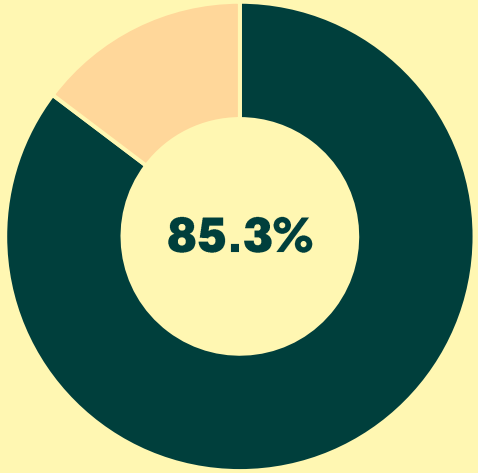
AUC (n=57)

Reference range modeling
9.98% optimal cutoff



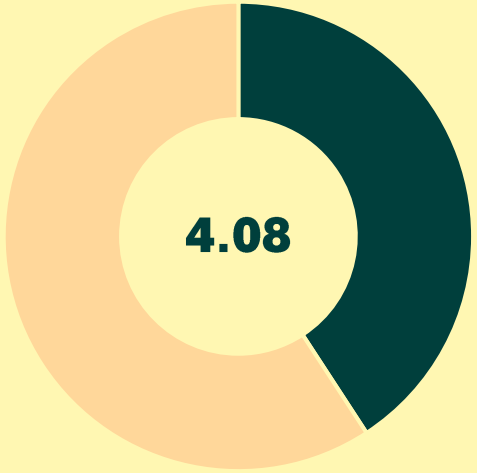
Sensitivity

Beta-cell injury detection
at 9.98% cutoff



Specificity

Healthy reference cohort at
9.98% cutoff



LOD (copies/µL)

Linearity 2.0E+03 → 1.25
R^2 > 0.9999 across range

Completed Validations

Accuracy & precision (5-day, ≤20% criteria) · Linearity (R^2 >0.9999) · LOD 4.08 c/µL · Recovery >60% · Carryover <0.8 c/µL · cfDNA stability 5 days

Controls: methylated / unmethylated human gDNA, mixed methylation standards, EndoC-βH5 beta-cell DNA, synthetic gBlocks, donor-derived cfDNA. Specificity confirmed by BLAST + HpaII digestion studies.

VALIDATION

Pediatric Stage 3 T1D cohort.

Multi-site collaboration with academic pediatric endocrinology programs.

Study Design

Subjects	15 pediatric patients with new-onset Stage 3 T1D
Sample type	EDTA plasma collected at hospital admission
Timepoint	Single draw at clinical presentation
Comparators	HbA1c, glucose, bicarbonate, BHB, autoantibody panel, DKA status
Assay	Kihealth Beta Test™ — unmethylated INS cfDNA via ddPCR
Lab	CLIA / COLA-certified Kihealth laboratory

Headline Findings

73%

detection rate at single timepoint

11 of 15

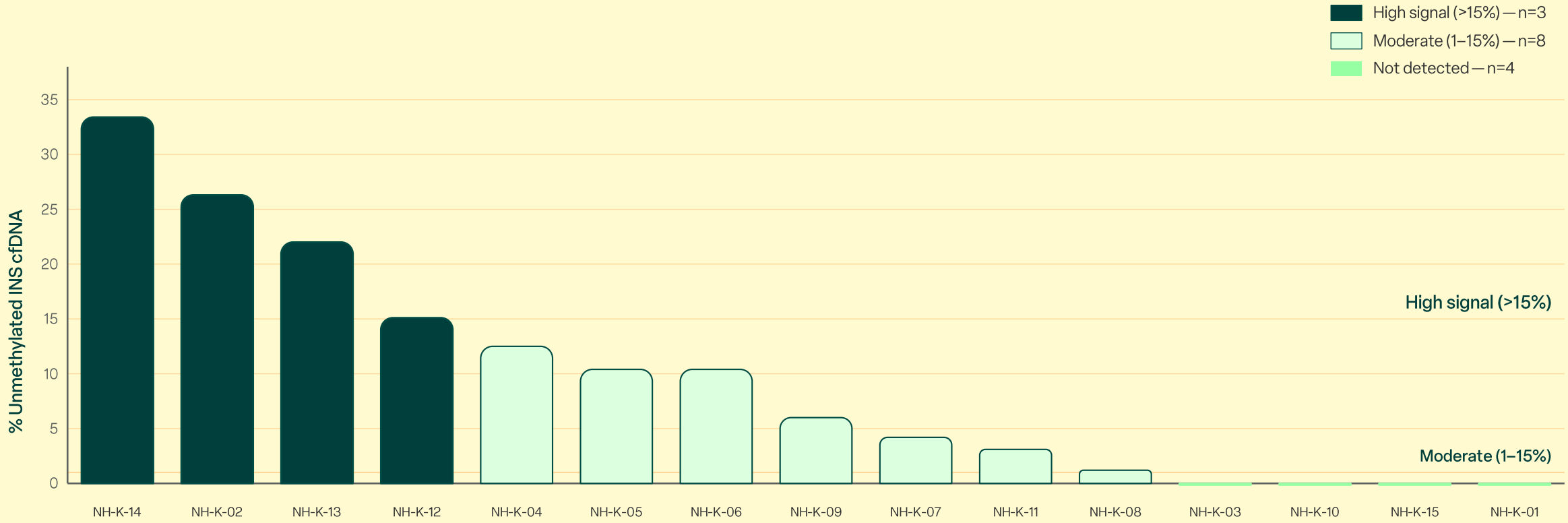
subjects with measurable unmethylated INS cfDNA signal at clinical presentation, despite the heterogeneity of metabolic state.

Conservative single-timepoint floor — signal modeling predicts >90% with serial sampling.

Individual cfDNA signals by subject.

Stage 3 T1D cohort (n=15) — single timepoint at admission, ranked by % unmethylated INS cfDNA.

Stage 3 T1D Pediatric Cohort (n=15)
73% detection rate · stratification independent of HbA1c, DKA status



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A new patient stratification axis.

cfDNA signal stratifies Stage 3 T1D patients independent of standard metabolic markers — opening a non-redundant decision variable.

HIGH SIGNAL

> 15% cfDNA

n - 3

14.5%
Mean HbA1c

60%
DKA rate

Active destruction + likely residual β-cell mass → Prime intervention candidates

MODERATE SIGNAL

1 – 15% cfDNA

n - 8

12.7%
Mean HbA1c

17%
DKA rate

Active destruction detected → Likely intervention candidates

NOT DETECTED

0% cfDNA (single draw)

n - 4

14.9%
Mean HbA1c

50%
DKA rate

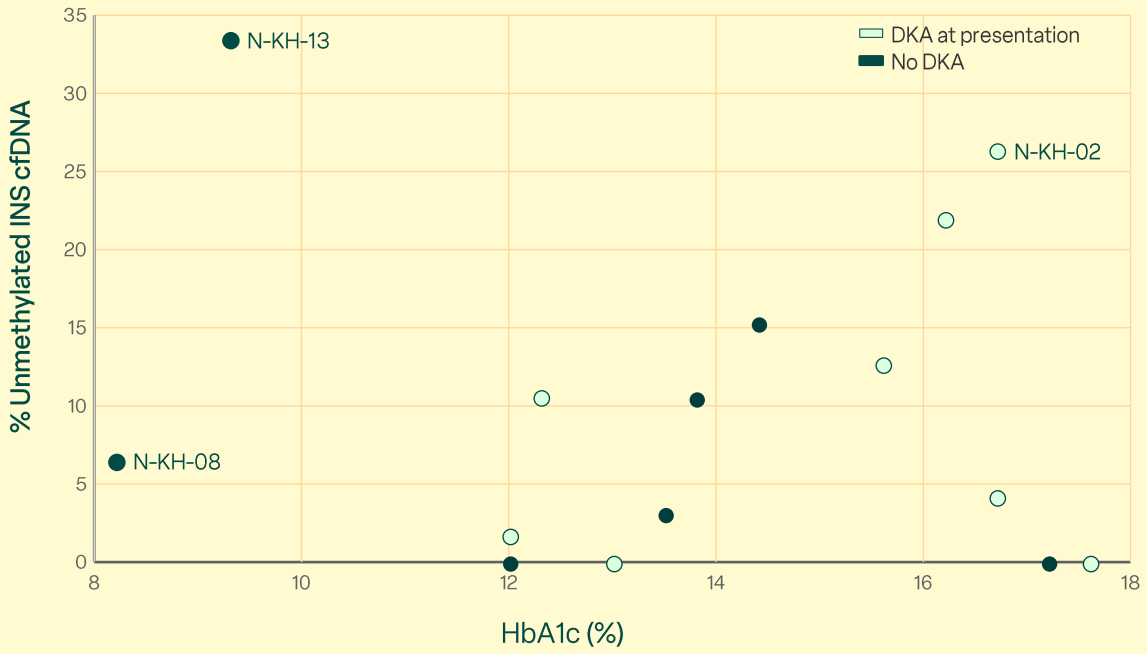
No active destruction at sampling → Limited residual mass likely; serial testing recommended

Stratification cutoffs derived from Stage 3 T1D pediatric cohort — pending validation in additional cohorts.

Independent of hba1c and DKA.

cfDNA signal provides non-redundant information — orthogonal to metabolic severity.

cfDNA Signal is Independent of HbA1c
No correlation with metabolic severity — non-redundant information



Clinical Implications

Severe ≠ Salvageable

Some subjects with very high HbA1c (16.7%) show high cfDNA — meaning active destruction is ongoing and intervention may still preserve residual mass.

Mild ≠ Early intervention

Some subjects with low HbA1c (8.2%) show measurable cfDNA — confirming β-cell death has already begun and supporting early therapy initiation.

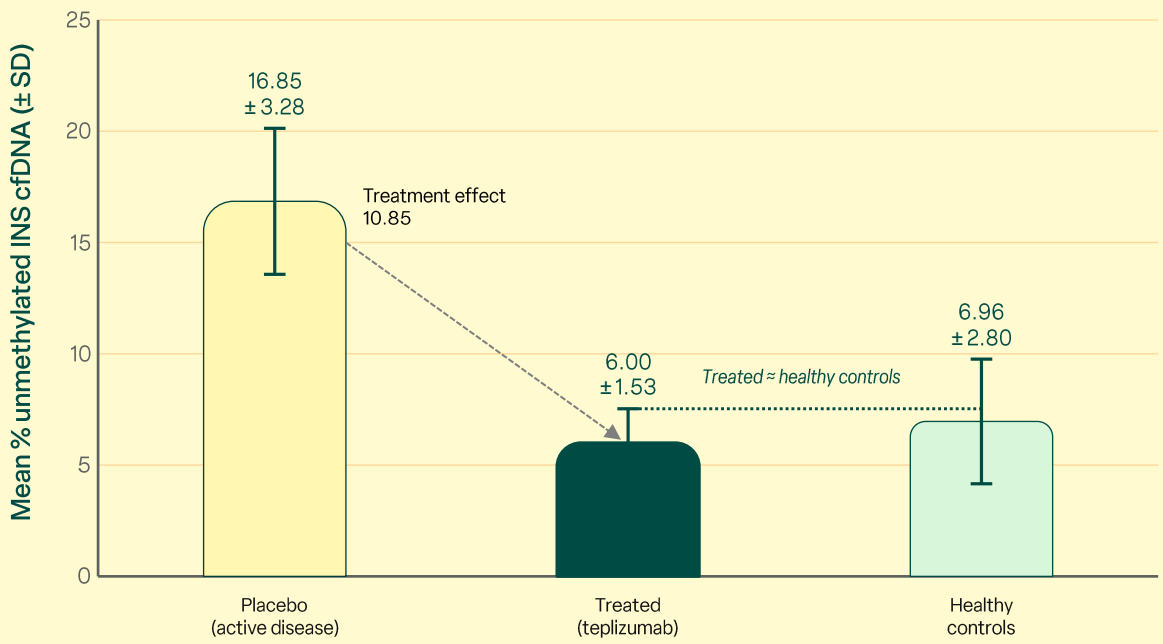
Showcase: N-KH-13

Highest cfDNA (33.5%) with lowest HbA1c (9.5%) — clinically appears mild, biologically the most active destruction in the cohort.

Treatment response: placebo vs treated vs HC.

Blinded longitudinal teplizumab samples — provided by Dr. Herold (Yale).

Teplizumab Treatment Response
Placebo vs Treated vs Healthy Controls (data from Kihealth ADA 2026 poster)



Key Observations

Placebo: 16.85 ± 3.28%
Untreated active disease — significantly elevated unmethylated INS cfDNA above healthy reference.

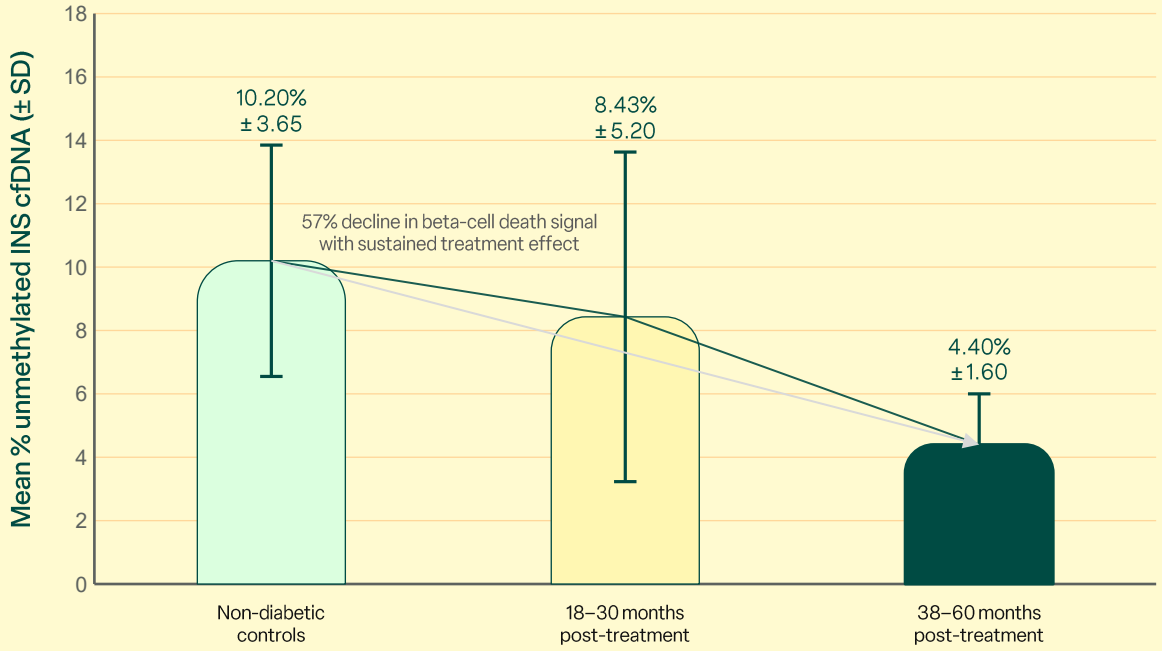
Treated: 6.00 ± 1.53%
Teplizumab-treated patients — substantial reduction reflecting therapeutic effect on beta-cell death.

Healthy controls: 6.96 ± 2.80%
Treated values closely match healthy baseline — biologically coherent response signature.

Long-term post-treatment response.

Sustained reduction in beta-cell death signal across 18–60 months post-treatment.

Long-Term Post-Treatment Response
Reduction in beta-cell death signal maintained over years



Endpoint Timing

Cohort	Mean cfDNA (± SD)
Non-diabetic controls	10.20 ± 3.65%
18–30 mo post-tx	8.43 ± 5.22%
38–60 mo post-tx	**4.40 ± 1.60%**

Faster endpoint = smaller, faster trials. Adaptive dose selection.
Earlier go/no-go decisions for emerging immune therapies.

Where this fits in clinical research.

PREVENTION TRIALS

Enriched Enrollment

Identify which autoantibody-positive subjects are actively progressing — select for treatment, deselect slow progressors.

INTERVENTION TRIALS

Real-Time PD Endpoint

Companion biomarker for teplizumab, anti-CD3, and other immune modulators. Shorter trials, faster decisions.

SCREENING

Pediatric prevention

Newborn cohort add-on, family screening for first-degree relatives. Companion to autoantibody panels.

MECHANISM

Active Disease Assay

First in vivo measurement of β-cell turnover. Tool for natural-history cohorts (TrialNet, TEDDY, DAISY).

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Thank You

Questions Welcome.

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Institutional Collaborators

Yale University · Diabetes Research Institute (Miami) · University of Florida · Anschutz Medical Campus · CHOC Children's · Nemours Children's Health · Mayo College of Medicine

Scientific Advisors

Camillo Ricordi, MD (Miami DRI) · Kevan Herold, MD (Yale) · Eitan Akirav, PhD (Harvard, former Yale) — Their foundational work on cfDNA methylation made this assay possible.

The Kihealth Team

Clifford Morris, PhD · Matthew Benson, MD · Robert E. Mons III · Pat Nasshorn · And the entire Kihealth lab team.