Uppsala IST
Type 1 Diabetes Data Conference Call

January 7, 2025

Sana Biotechnology®

Cautionary Note Regarding Forward-Looking Statements

This presentation contains forward-looking statements about Sana Biotechnology, Inc. (the "Company," "we," "us," or "our") within the meaning of the federal securities laws. All statements other than statements of historical facts contained in this presentation, including, among others, statements regarding the Company's strategy, expectations, cash runway and future financial condition, future operations, and prospects, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. The Company has based these forward-looking statements largely on its current expectations, estimates, forecasts and projections about future events and financial trends that it believes may affect its financial condition, results of operations, business strategy and financial needs. In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. These statements are subject to risks and uncertainties that could cause the actual results to vary materially, including, among others, the risks inherent in drug development such as those associated with the initiation, cost, timing, progress and results of the Company's current and future research and development programs, preclinical studies, and clinical trials.

For a detailed discussion of the risk factors that could affect the Company's actual results, please refer to the risk factors identified in the Company's SEC reports, including its Quarterly Report on Form 10-Q dated November 8, 2024. Except as required by law, the Company undertakes no obligation to update publicly any forward-looking statements for any reason.

Introduction

Steve Harr, MD

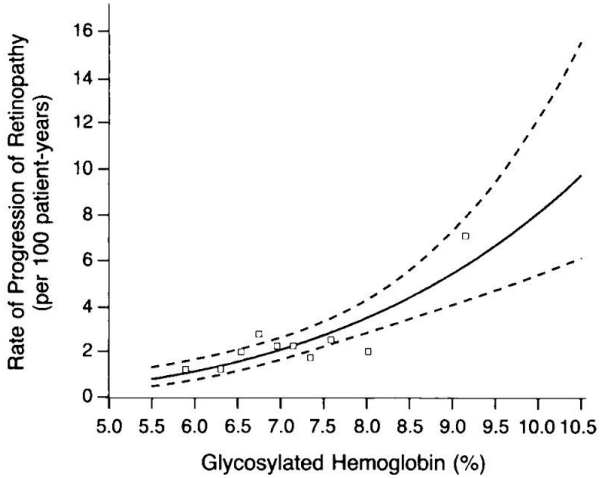
Sana's goal is to scale access to engineered cell therapies with curative intent

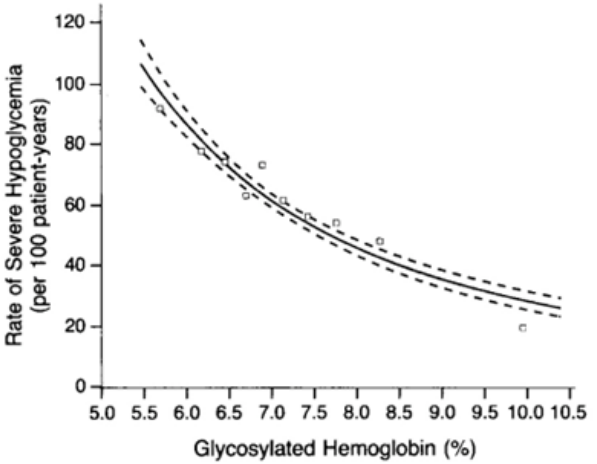
- The impact of *ex vivo* engineered cell therapy has been limited by the challenges of immune rejection of allogeneic cells
  - Autologous cell therapy is limited in both scale and types of cells
  - Immunosuppression with allogeneic cells/organs has significant safety and tolerability challenges
- Our hypoimmune platform (HIP) is designed to overcome rejection of allogeneic cells. It also appears to overcome immune recognition in a number of autoimmune disorders
- Preclinical data, including in NHP, have provided direct evidence that HIP-edited cells overcome allogeneic immune rejection. Early clinical data with allogeneic CAR T cells have been supportive
- We and our partners at Uppsala designed the current investigator-sponsored trial to study whether HIP-edited primary islet cells can evade immune detection, survive, and function in a patient with type 1 diabetes
- The study achieved its goal, making us optimistic that a one-time treatment in a patient with type 1 diabetes with HIP-modified, stem-cell derived islets has the potential to lead to normal blood glucose without insulin or immunosuppression
- We believe the immune evasion observed in the study is generalizable across many cell types as we continue work across our portfolio

Type 1 diabetes (T1D) introduction

- T1D is caused by autoimmune destruction of insulin-producing beta cells in the pancreas and results in hyperglycemia, requiring lifelong insulin therapy
- 8.4M people worldwide have T1D. Incidence is increasing annually, and the prevalence is expected to double over the next 15 years
- 80% of individuals with T1D are from high-income countries
- Insulin therapy was discovered ~100 years ago, and it has been transformative for patients. However, it is not curative, and patients and their families must be constantly vigilant for both hyperglycemia and hypoglycemia
- T1D leads to more than a decade shorter life expectancy despite significant advances such as continuous glucose monitoring, insulin pumps, and novel forms of insulin
- Complications directly related to hyperglycemia include microvascular (retinopathy, nephropathy, neuropathy) and macrovascular (coronary artery disease, heart attacks, stroke, poor wound healing, and amputations) issues
- At the other extreme, severe hypoglycemia can be rapidly fatal

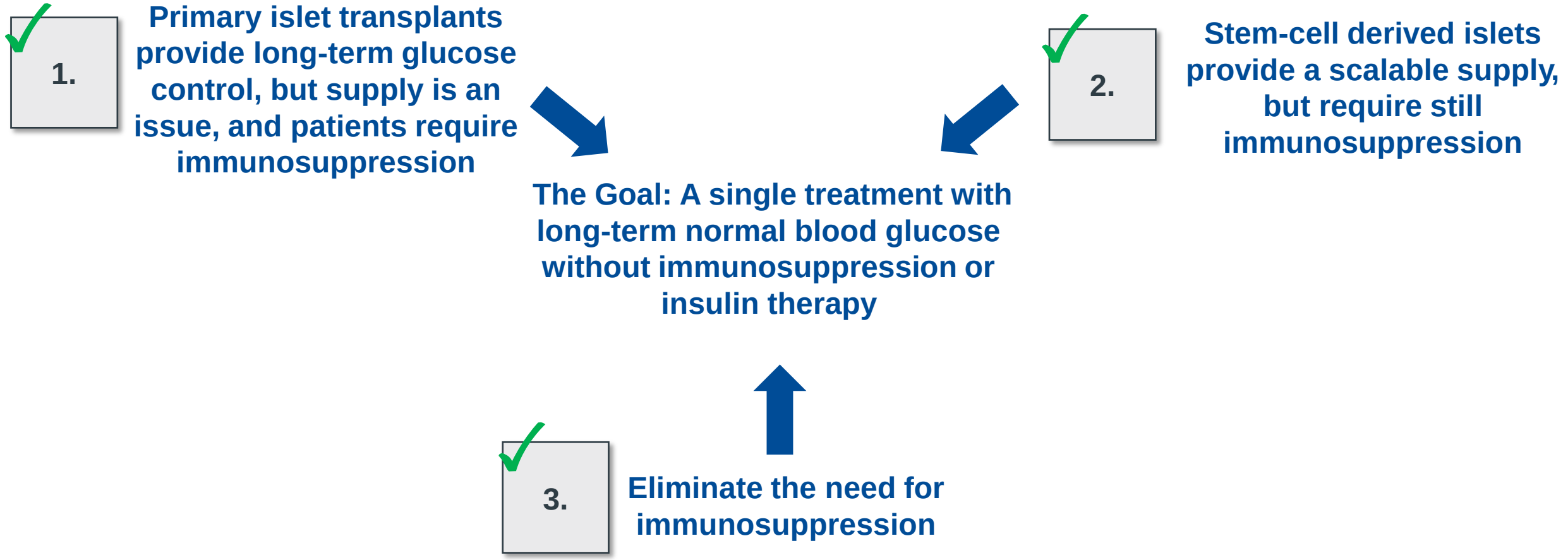
Improvement in glycemic control reduces microvascular complications but increases the risk of hypoglycemia[1]





1. Diabetes Control and Complications Trial Research Group et. Al. N Engl J Med 1993; 329:977-986

Advancing Toward A T1D Cure For Broad T1D Population

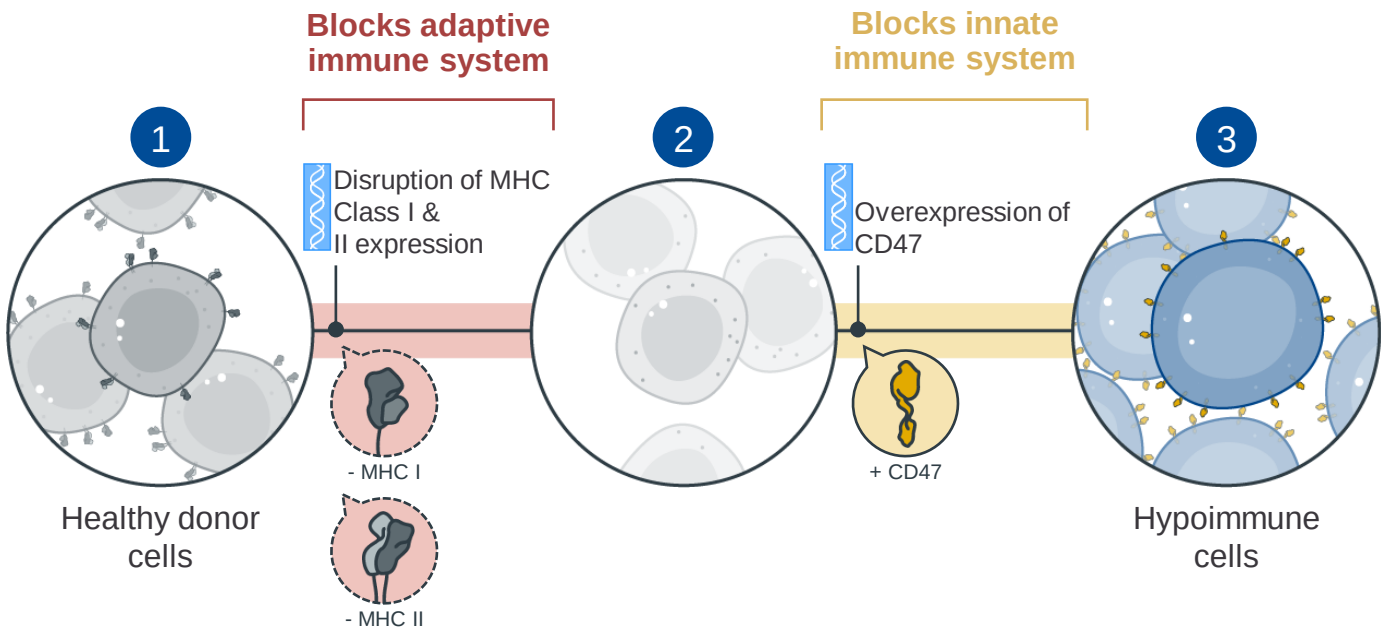


Overcoming allogeneic immune rejection has been key limitation in transplant and cellular medicine

Allogeneic cell rejection

- ~75 years of transplants – immune rejection remains the largest problem
- Lifelong immunosuppression is current standard
- Genome modification efforts to date have generally been incomplete
- Autologous therapies have limited scalability and are only available for a small number of cell types

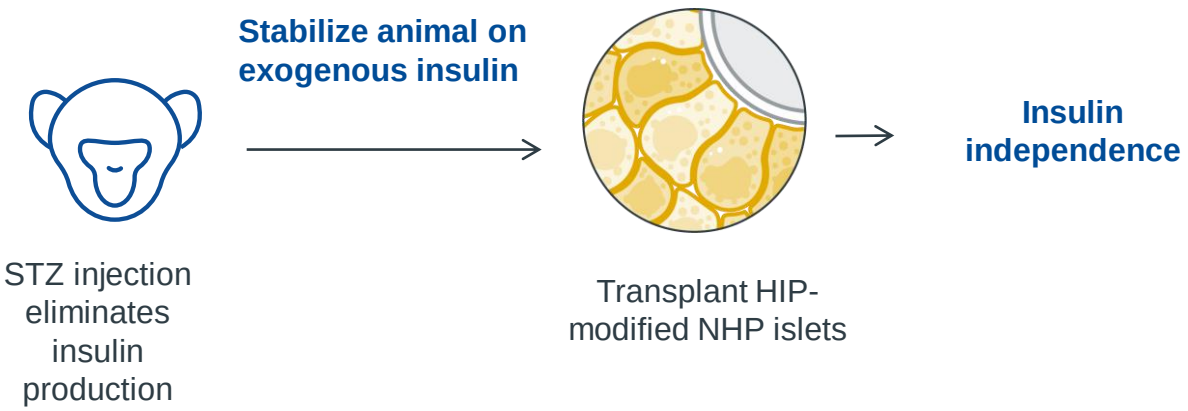
Sana's hypoimmune approach



Current clinical platform with multiple ongoing approaches in research phase.

Preclinical study showed HIP-modified allogeneic islet cells can control glucose in an NHP model

Type 1 diabetes is a disease of missing pancreatic beta cells



Study Design (N=1)

- NHP treated with STZ
- Glucose stabilized with exogenous insulin
- Allogeneic NHP primary islet cells isolated and HIP-modified
- Cells injected intramuscularly without immunosuppression

Key goals of study

- Demonstrate survival and function of HIP-modified allogeneic islet cells in diabetic NHP without immunosuppression
- Demonstrate long-term glucose normalization in diabetic NHP without exogenous insulin or immunosuppression
- Demonstrate the principle of graft ablation/safety switch with anti-CD47 antibody

Abbreviations: NHP, non-human primate; STZ, Streptozotocin

Hu et al., 2024, Cell Stem Cell 31, 334–340

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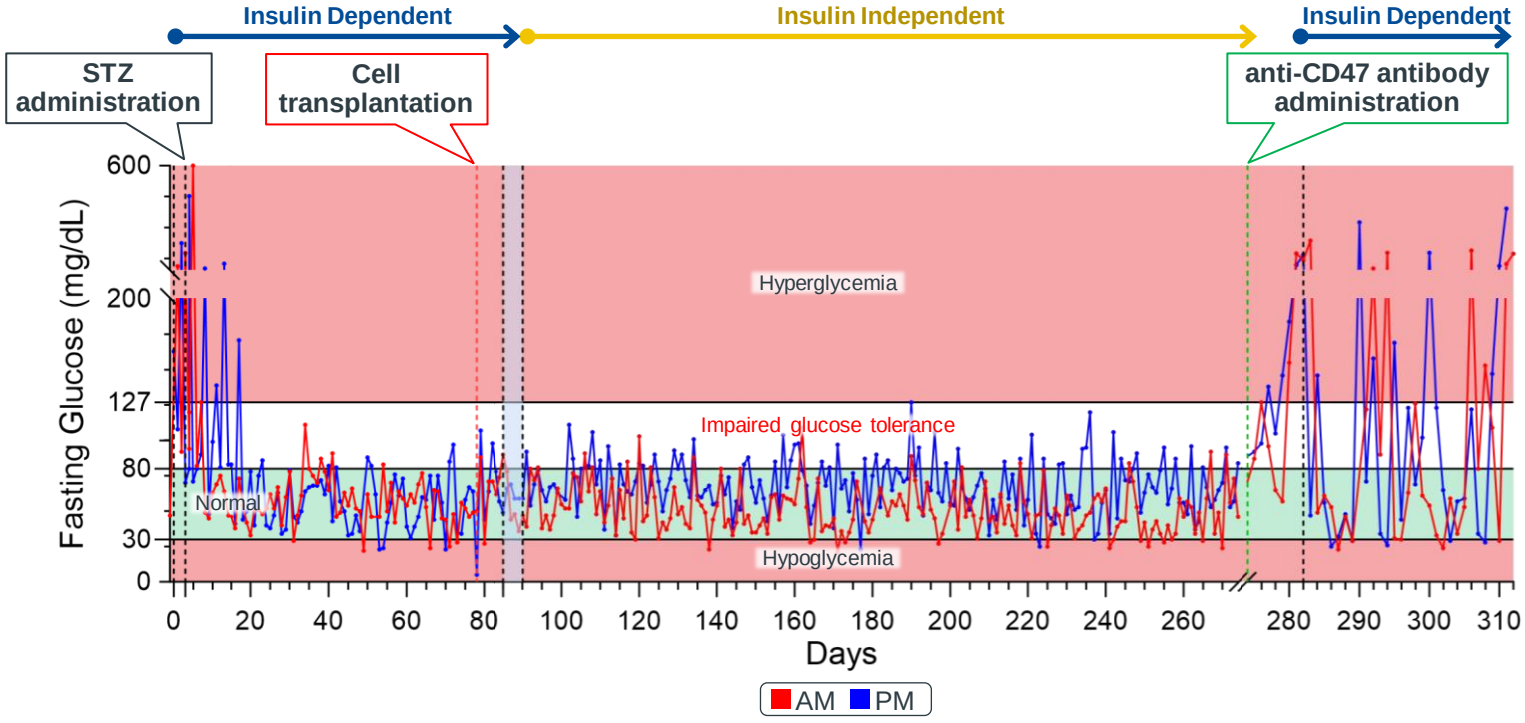
Preclinical study: survival & function of allogeneic hypoimmune pancreatic islet cells in diabetic NHP 6 months without immunosuppression

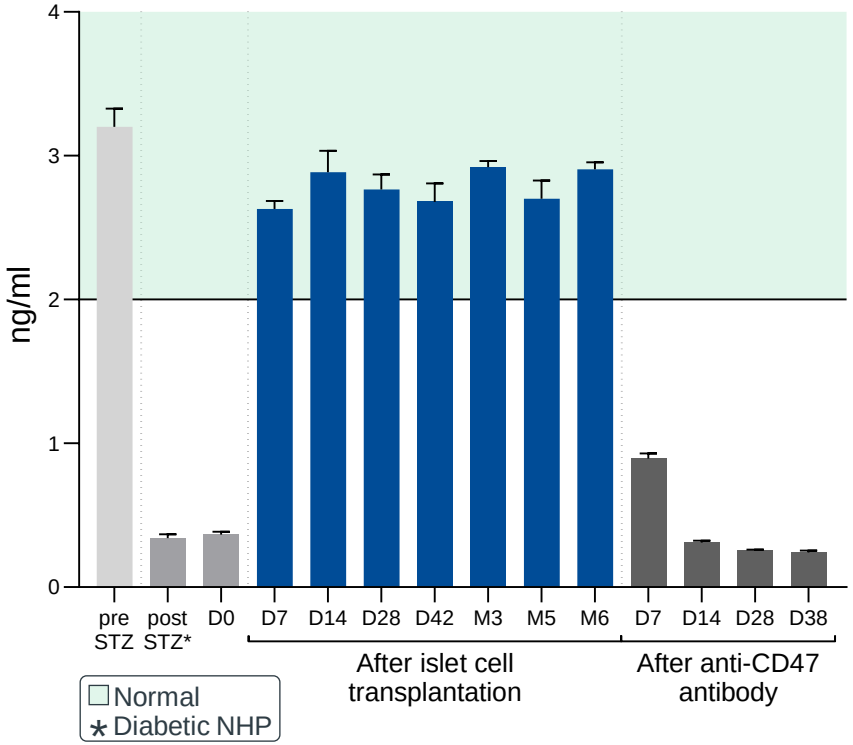
Study Design (N=1)

- NHP primary islet cells isolated and HIP-modified
- Cells injected intramuscularly into a diabetic, allogeneic NHP without immunosuppression

Fasting glucose



Serum C-peptide



Hu et al., 2024, Cell Stem Cell 31, 334–340

UP421 – World's first HIP-edited primary islet transplantation

Interim Analysis 4 weeks after transplantation

Sonja Schrepfer, MD, PhD
on behalf of the Sana Team and the Uppsala/Oslo Team

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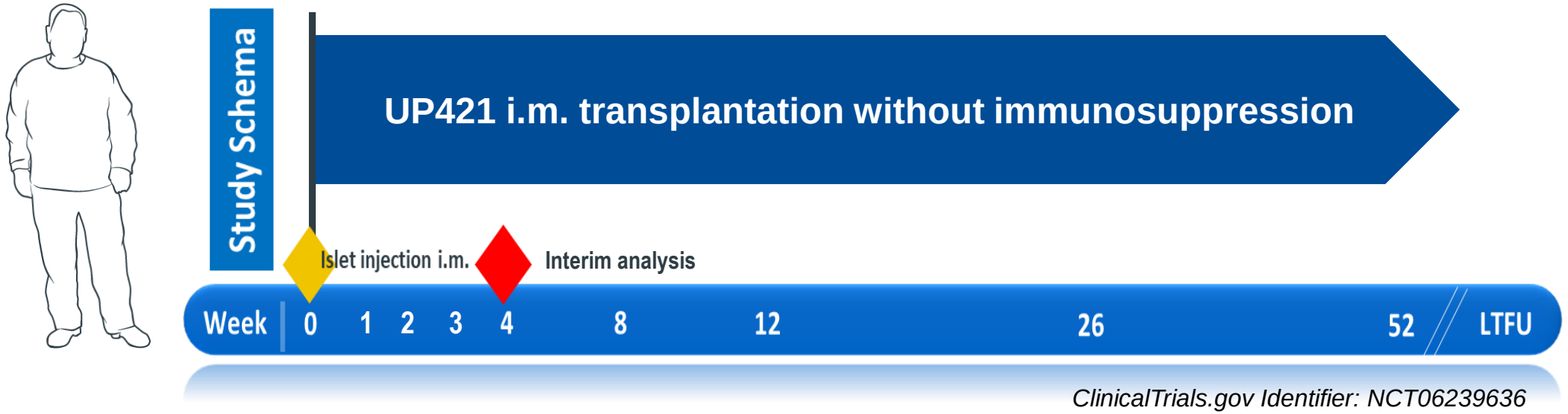
Note: Some data are verbally reported values and could slightly differ from CRF (which will show final documented values). The Leona M. and Harry B. Helmsley Charitable Trust generously provided support for the clinical trial.

Clinical study design

First-in-human safety study of allogeneic HIP pancreatic islet transplantation in adult patient with type 1 diabetes (no immunosuppression)



ClinicalTrials.gov Identifier: NCT06239636

Study details

Study: Single arm, open label, Ph1 IST, 1 patient

Product: ATMP (UP421) with allogeneic, HIP islet cells

Primary endpoint: Safety (number of treatment-related adverse events, CTCAE grade ≥3)

Secondary endpoints: Immune evasion and cell survival (stable C-peptide and signal in MRI)

Dose: 25-80M. *To focus on safety, trial dose will be between 2% and 7% of islet cells needed for insulin independence in intraportal location*[1,2]

Location: intramuscular (IM; forearm muscle)

Sponsor: Uppsala University Hospital (PI: Dr. Per-Ola Carlsson)

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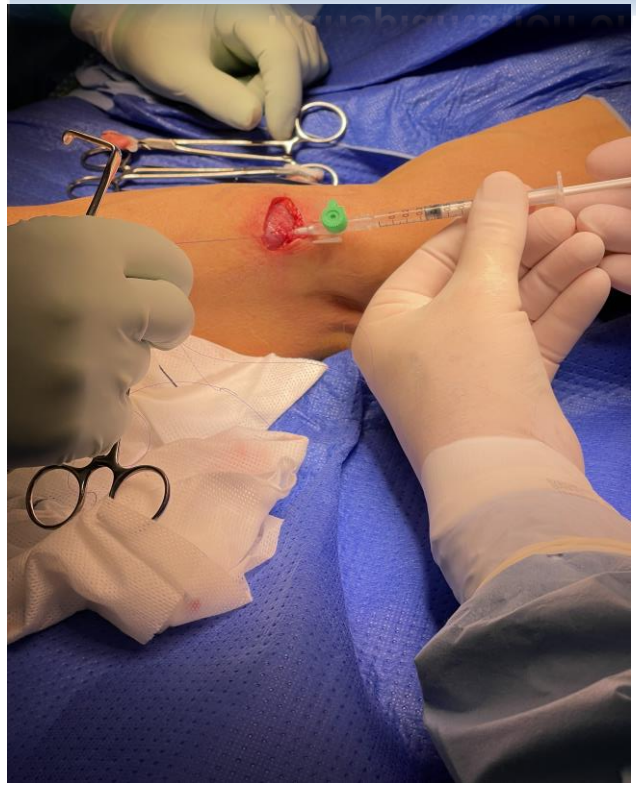
1. Shapiro A.M. James et al. N Engl J Med 2000.343:4; 230-238. 2. Pisania A et al. Laboratory Investigation 2010;90:1661–1675.

Key Details

Parameter	Donor Information
Blood type	O+
Ischemia time	5 hours 11 mins
Gender	male
Age	61
Islet Purity	86%
HbA1c	42mmol/l (6%)

Parameter	Recipient Information
T1D diagnosis	1987
Blood type	O+
Gender	male
Age	42
HbA1c	96mmol/l (10.9%)

Transplantation on December 2nd, 2024



Procedure performed at Uppsala University Hospital took 90 mins

AKADEMISKA SJUKHUSET

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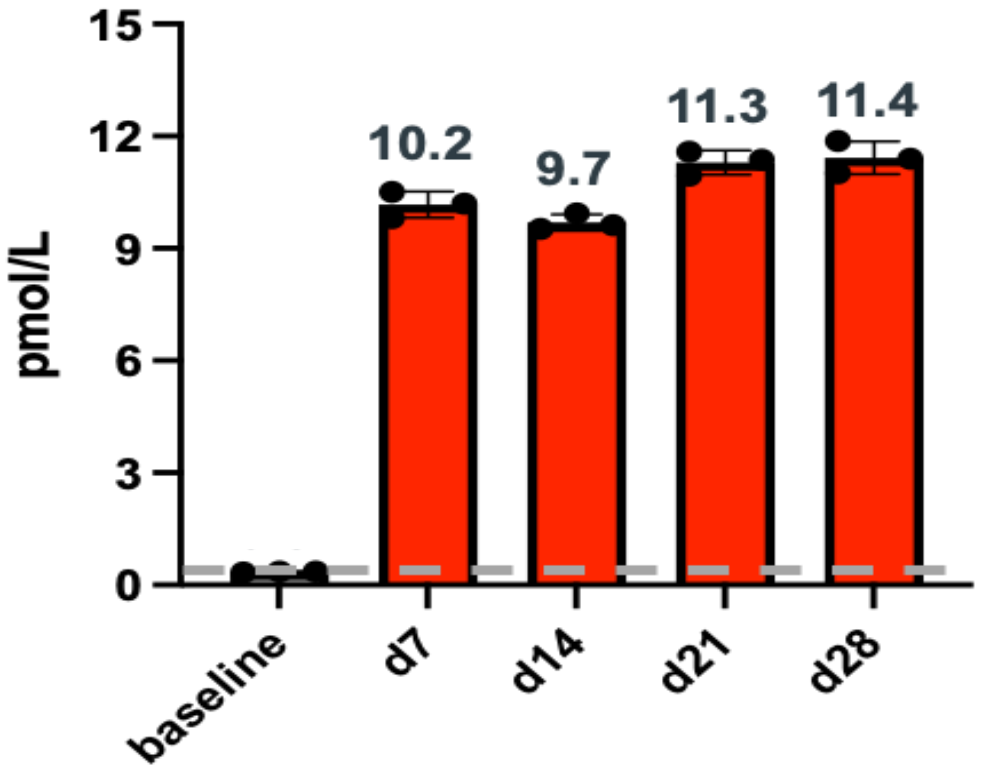
Primary and Secondary Endpoints - Data Summary

All interim primary and secondary endpoints were met

Endpoints	D7	D14	D21	D28
Safety (no AE/SAE related to drug)	✓	✓	✓	✓
Cell survival/function (C-peptide)	✓	✓	✓	✓
Graft visibility (MRI)	✓	✓	Not performed (as per protocol)	✓
Adaptive immune evasion	✓	✓	✓	✓
Innate immune evasion	✓	✓	✓	✓

Stable C-peptide after HIP islet cell transplantation demonstrates survival and function of cells

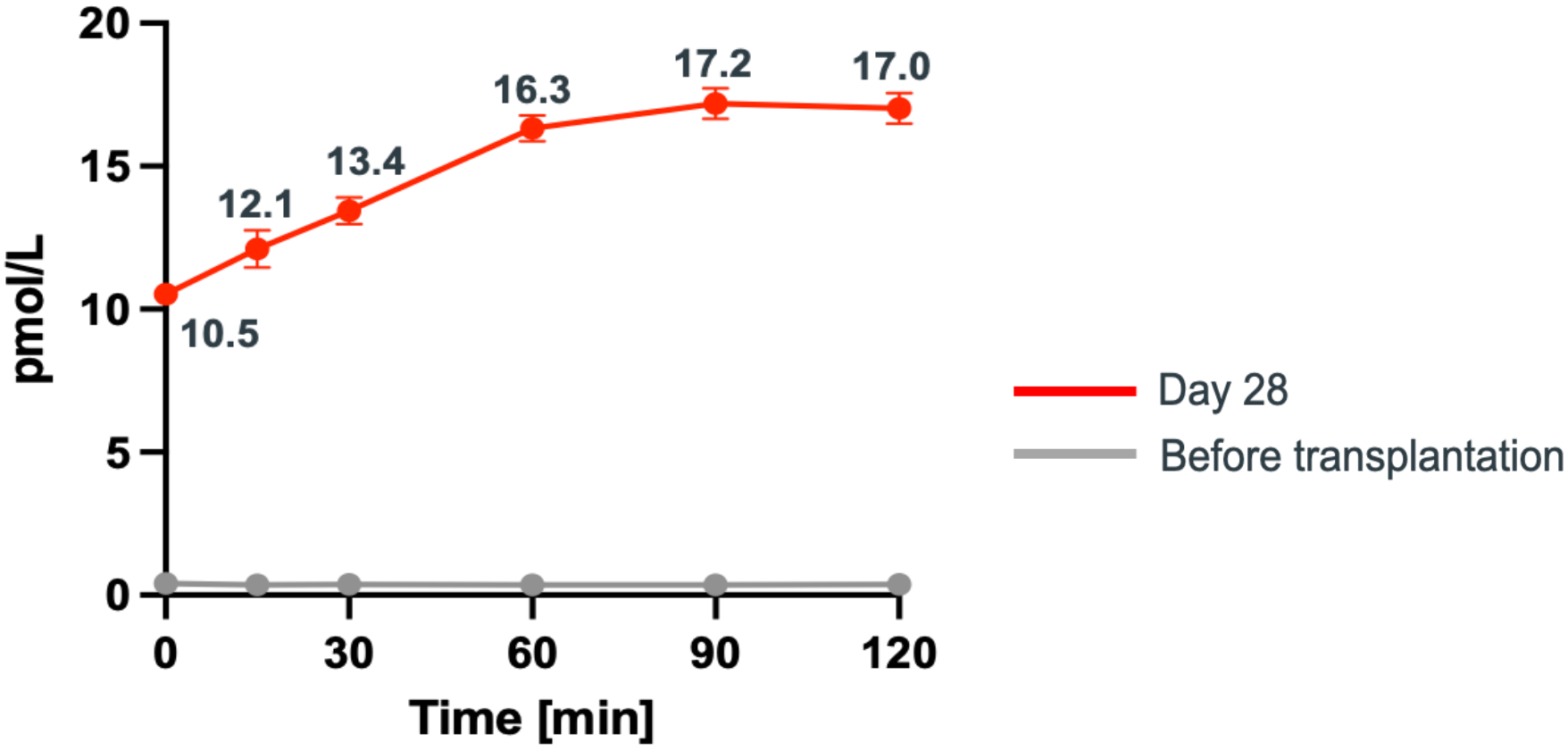
Basal C-peptide in peripheral blood



Summary: No detectable C-peptide before transplantation; present and stable C-peptide observed after transplantation.

Baseline: Below limit of detection (LOD).Sensitivity: 0.48 pmol/L.
Dots represent technical triplicates. C-peptide analyzed in serum.

Increased C-Peptide Levels with a Mixed Meal Tolerance Test (MMTT) after transplantation

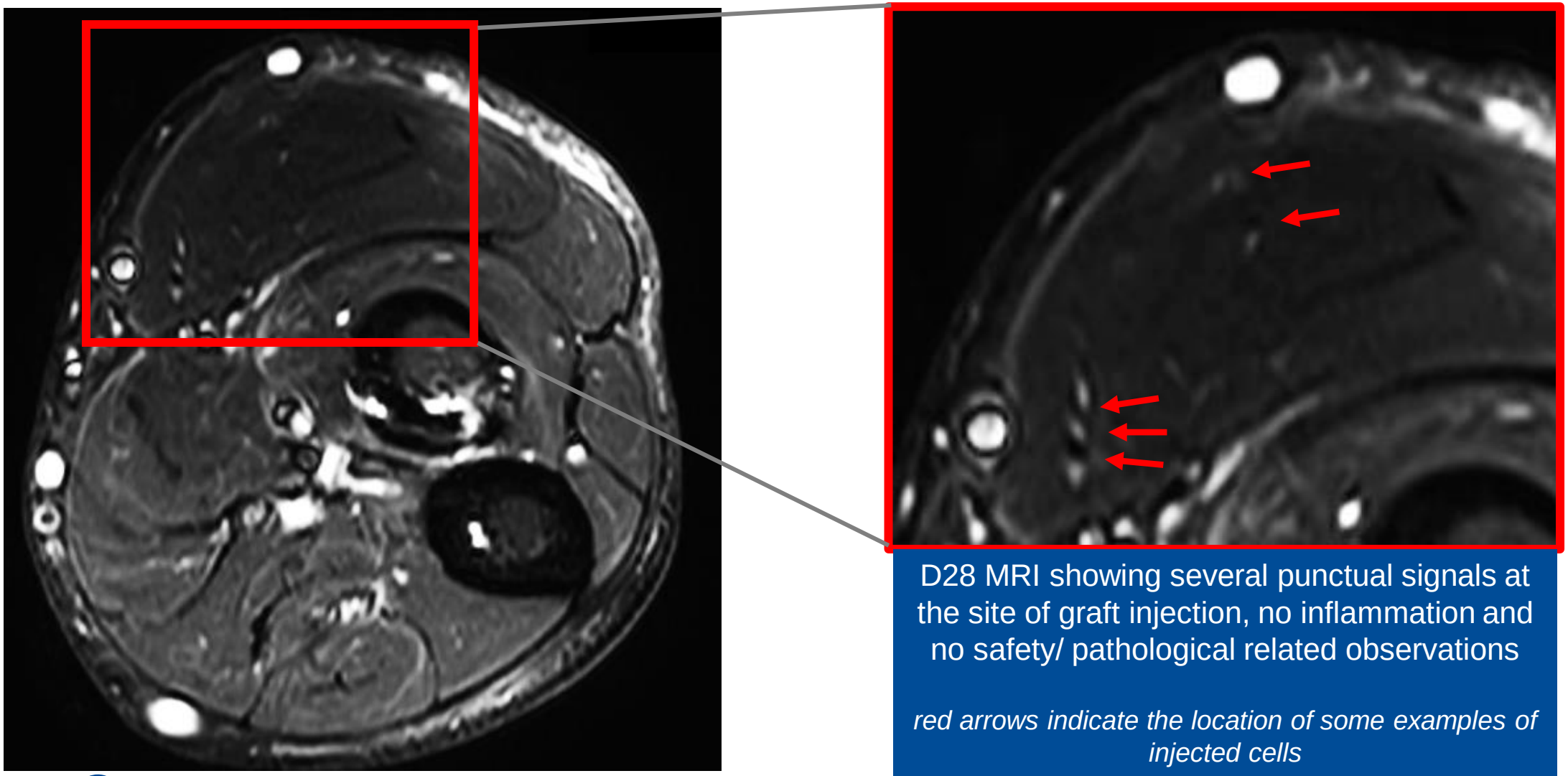


Summary: Pre-transplantation, C-peptide is below detection limit during MMTT. 28 days after UP421 transplantation, C-peptide is present and stimulated by MMTT.

Baseline: Below limit of detection (LOD).Sensitivity: 0.48 pmol/L.
Standard deviation represent technical triplicates. C-peptide analyzed in plasma samples.

Day 28 MRI showing further evidence of graft survival

MR T2-STIR-weighted trans images showing signal in musculus brachioradialis after injection of UP421



D28 MRI showing several punctual signals at the site of graft injection, no inflammation and no safety/ pathological related observations

red arrows indicate the location of some examples of injected cells

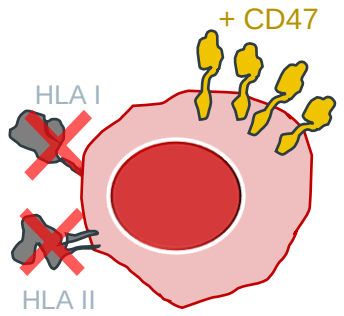
The MR T2-STIR-weighted sequence is sensitive to water and fluid and is a fat suppression technique to suppress the high signal from fat.

Immune analysis was performed using donor islet cells and patient's immune cells

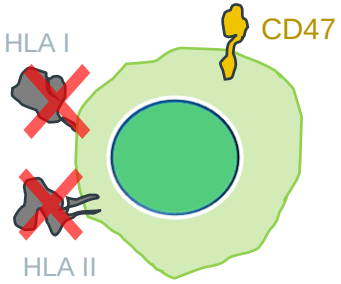
Mixed cell population in drug product allows for detailed immune analysis

Donor

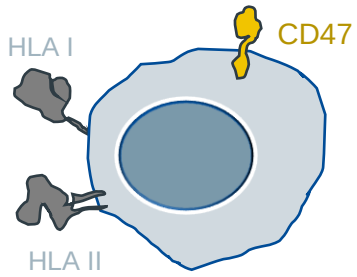
HIP islet cells



dKO islet cells



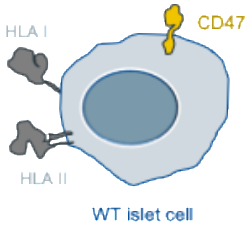
WT islet cells



Immune analysis using patient's (recipient) immune cells after transplantation

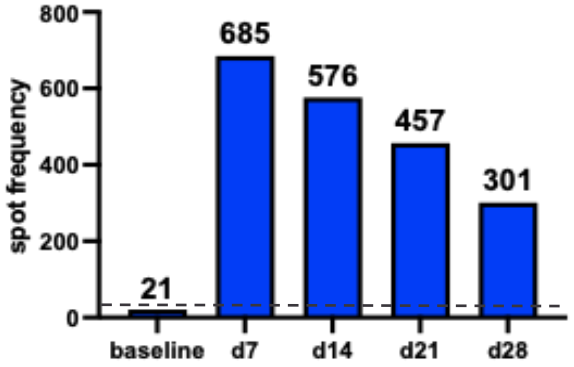
- **T cells**
- **Donor-specific antibodies**
- **Natural killer cells**
- **Whole blood**

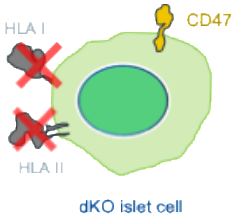
Adaptive Immunity: HIP islet cells evade patient's T cell response up to 28 days after transplantation



WT islet cell

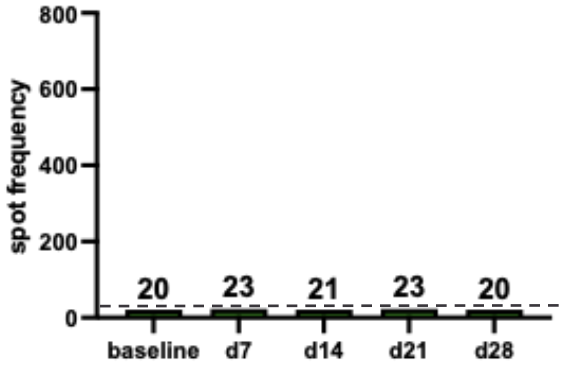
WT islet cells:
Patient's T cells are activated and kill WT islet cells with peak at 7 days after transplant

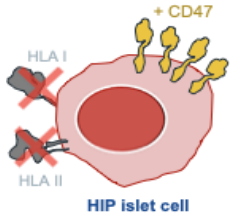




dKO islet cell

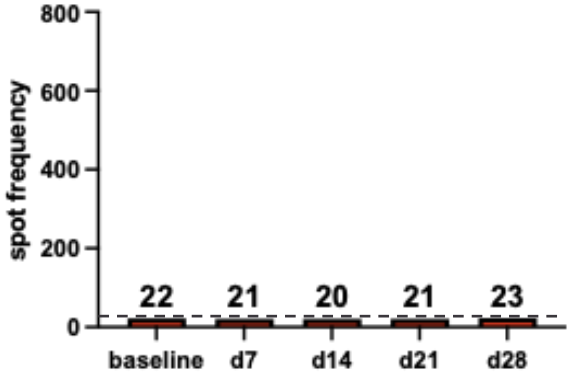
dKO islet cells:
No killing of HLA deficient cells by patient's T cells

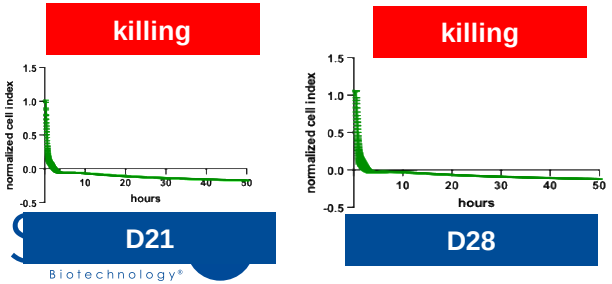


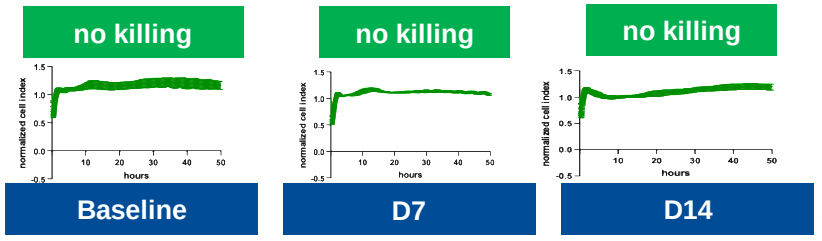


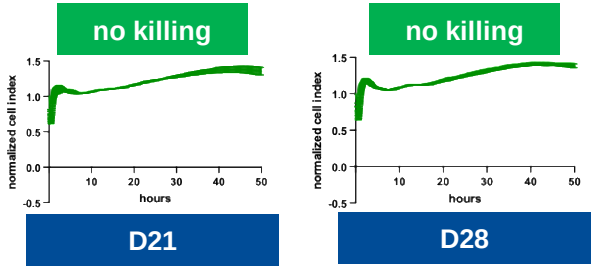
HIP islet cell

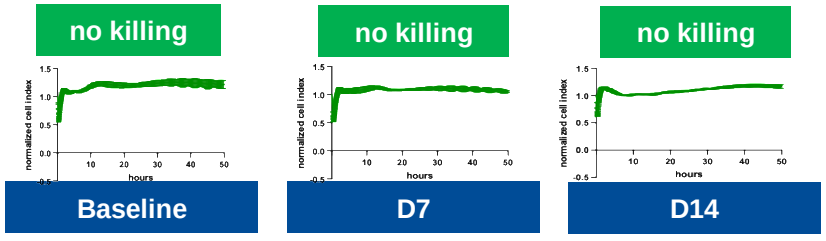
HIP islet cells:
No killing of HIP islet cells by patient's T cells

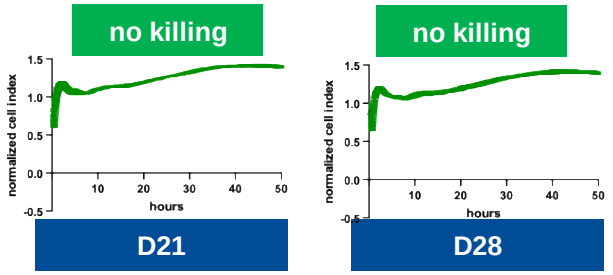




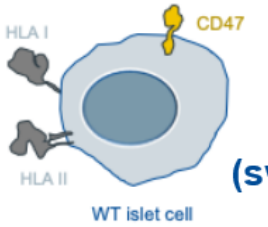




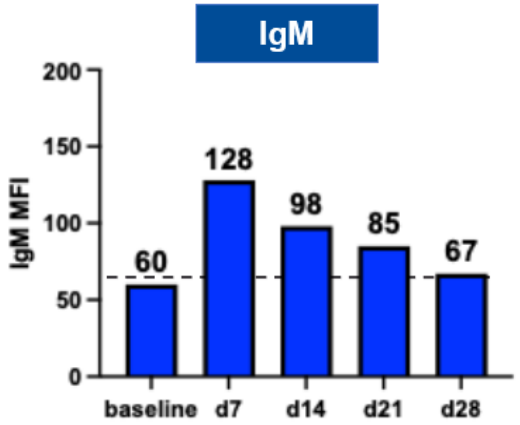


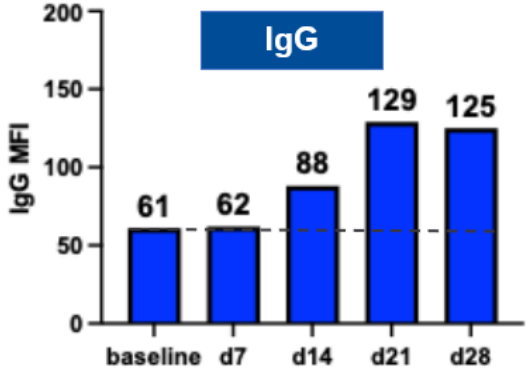


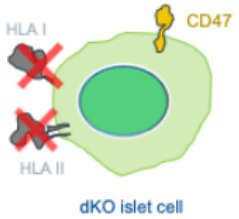
Adaptive Immunity: No patient donor-specific antibodies against HIP islet cells up to 28 days after transplantation



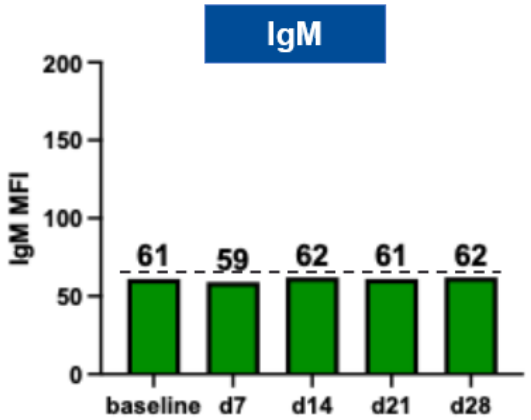
WT islet cells:
Patient's B cells produce donor-specific antibodies (switch from IgM to IgG at D14)

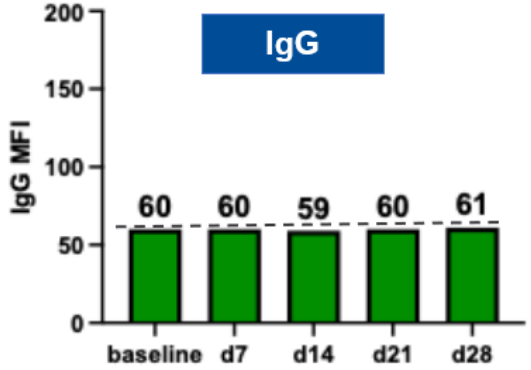


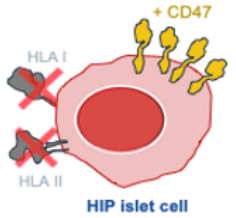




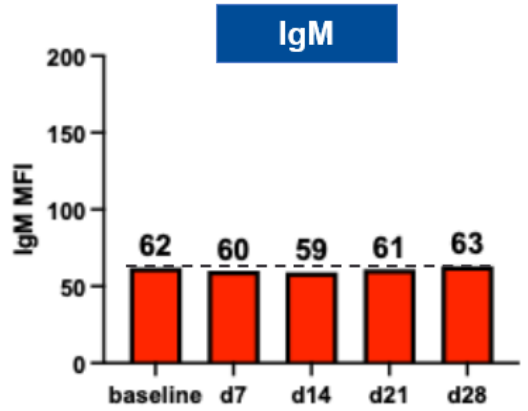
dKO islet cells:
No binding of donor-specific antibodies to HLA deficient cells

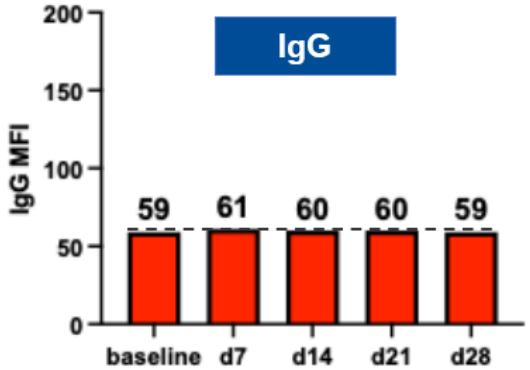






HIP islet cells:
No binding of donor-specific antibodies to HIP islet cells





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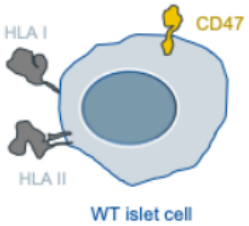
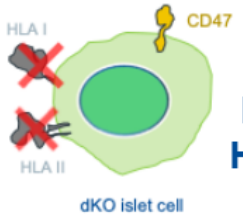
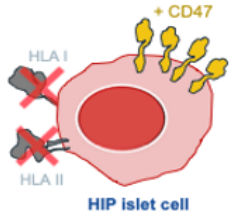
Innate Immunity: HIP islet cells evade patient's NK cell response up to 28 days after transplantation



WT islet cells:
No killing of WT cells by patient's NK cells



dKO islet cells:
Patient's NK cells are killing HLA I/II deficient cells (due to "missing-self")

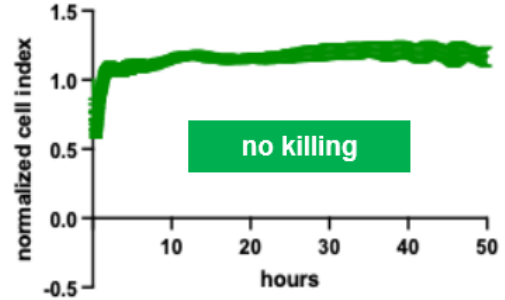


HIP islet cells:
No killing of HIP islet cells by patient's NK cells

Baseline

Baseline

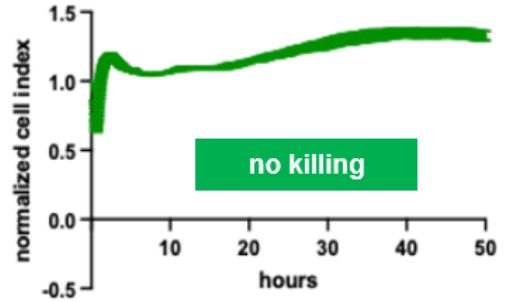
Baseline



D28

D28

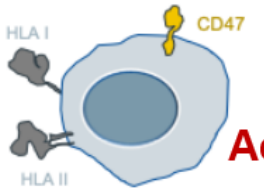
D28



Results from D7, D14, and D21 timepoints are similar to the D28 results in each assay.

Adaptive and innate immunity: No detectable immune response in the patient toward HIP islet cells

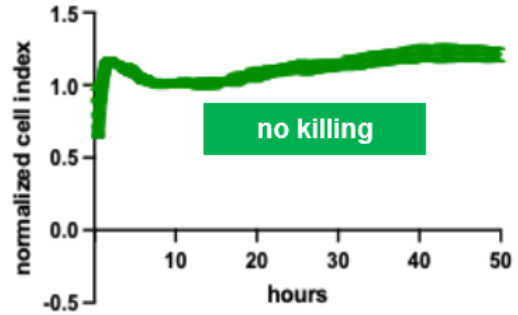
PBMC (containing all immune cell populations) plus serum (containing antibodies and complement) killing assay.



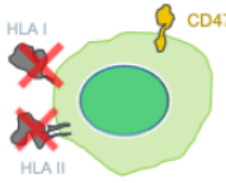
WT islet cells:
Adaptive immune killing

WT islet cell

Baseline



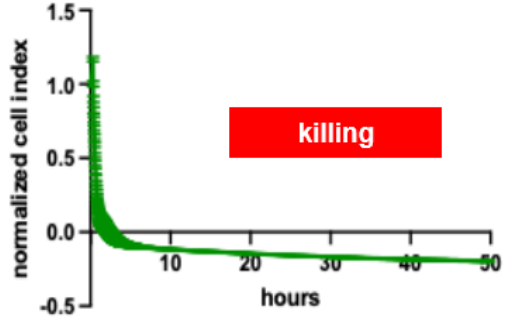
D28



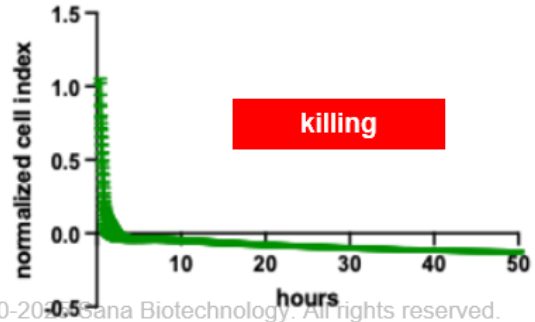
dKO islet cells:
Innate immune killing

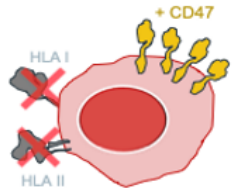
dKO islet cell

Baseline



D28





HIP islet cells:
No immune response

HIP islet cell

Baseline

D28

Results from D7, D14, and D21 timepoints are similar to the D28 results in each assay.

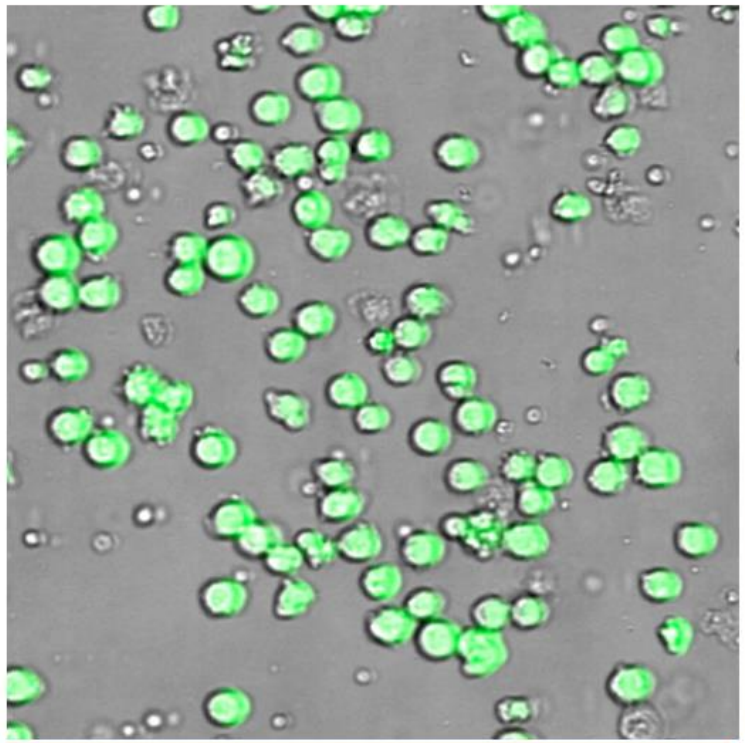
Video

HIP cells overcome patient's allogeneic and autoimmune barrier

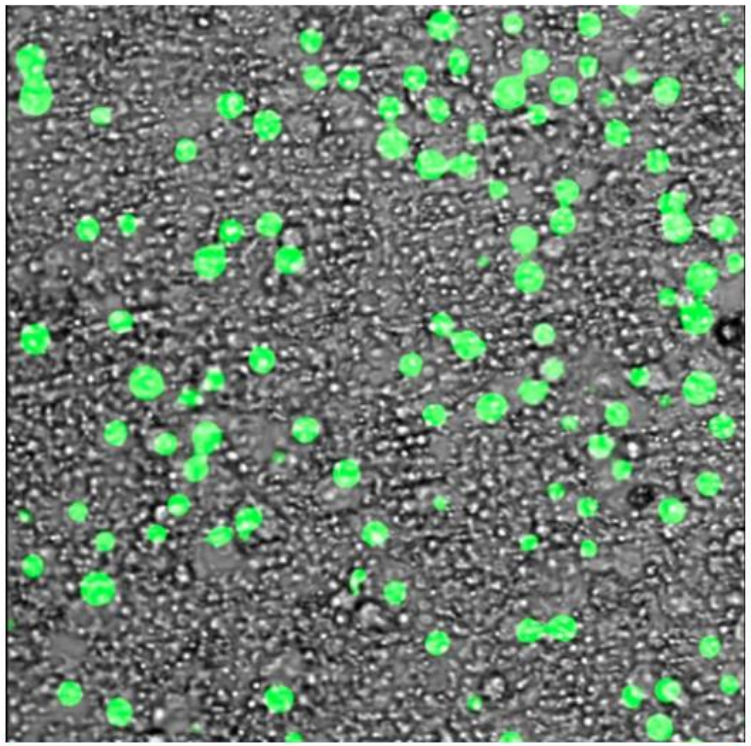
D7 sample. PBMC (containing all immune cell populations) plus serum (containing antibodies and complement) killing assay.

Still image before movie

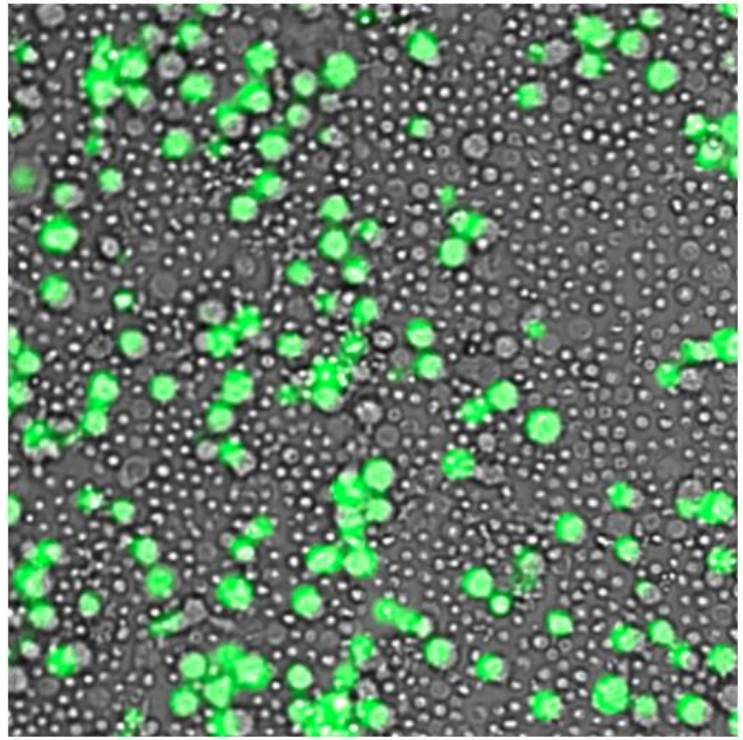
Target: WT islet cell	Target: HLAI/II dKO islet cell	Target: HIP islet cell



Adaptive immune Killing



Innate immune Killing



No immune killing

Actual assay time = 4 hours.

Donor islet cells with editing profile in column title

NK cells

Video

HIP cells overcome patient's allogeneic and autoimmune barrier

D7 sample. PBMC (containing all immune cell populations) plus serum (containing antibodies and complement) killing assay.

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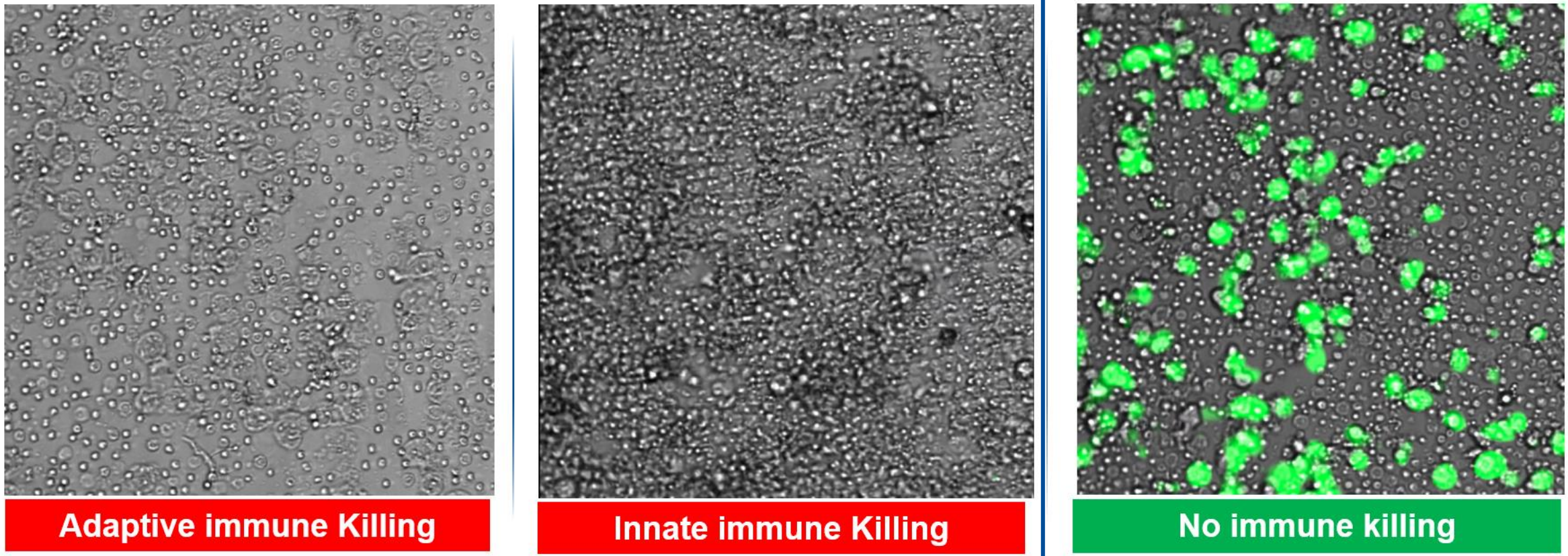
Target: WT islet cell	Target: HLAI/II dKO islet cell	Target: HIP islet cell



Adaptive immune Killing	Innate immune Killing	No immune killing

Actual assay time = 4 hours.

Donor islet cells with editing profile in column title

NK cells

Summary

- Transplantation of HIP primary islet cells is **safe** with no AE/SAE related to the drug product

- **Stable C-peptide** after transplantation and **increase after Mixed Meal Tolerance Test (MMTT)** demonstrate **survival** and **function** of HIP islet cells (supported by MRI)

- Drug product is a mixture of partially and fully gene edited islet cells:
  - Immune responses against all partially edited islet cells
  - **HIP** primary islet cells **evade allogeneic and autoimmune responses** in spite of rejection of partially edited islet cells

This first-in-human proof-of-concept study for the HIP platform shows that transplanted fully allogeneic islet cells survive and function without any immunosuppression.

Dec. 2nd with UP421

My hope for the future: Off-the-shelf therapies without the need for immunosuppression for Anyone, Anytime, Anywhere".

Sonja Schrepfer

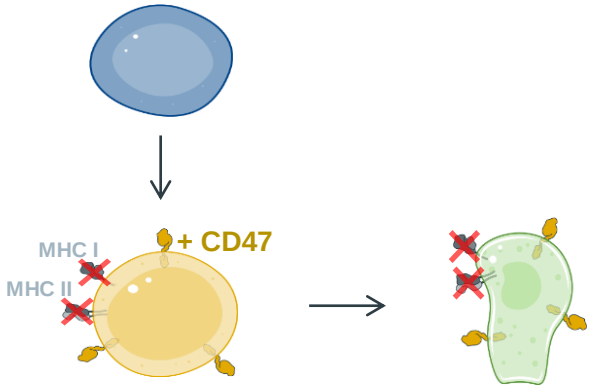
SC451 Program

Dhaval Patel, MD, PhD

Sana Biotechnology®

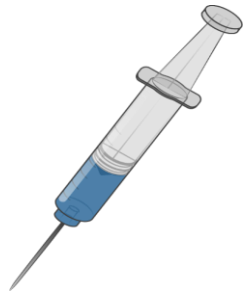
Sana’s approach to treat type 1 diabetes

1 Make hypoimmune islet cells from well-characterized PSC line



2 Manufacture at scale

3 Deliver as a one-time IM therapy without immunosuppression



SC451 program – HIP stem cell-derived islet cell therapy – delivered with no immunosuppression

- **We are taking the time to get it right the first time**
- **We believe that this therapy can transform the life of every type 1 diabetic if we can successfully develop and build the needed scale**

Four major challenges to realizing the vision of SC451

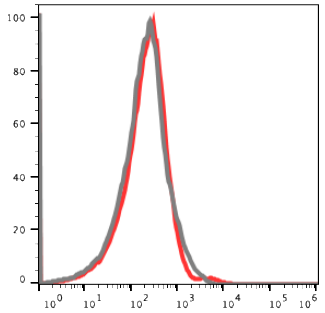
1. Overcoming immune rejection without immunosuppression.
   - We believe this challenge has now been solved.

2. Differentiating PSCs into islet cells at a purity, potency and yield to enable clinical trial dosing.
   - Many groups have done this successfully and so has Sana.

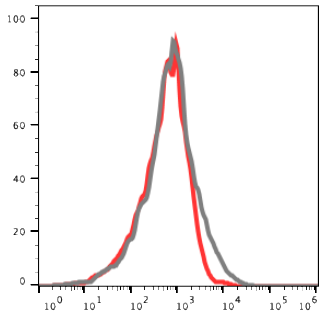
3. Generating a gene-modified master cell bank (MCB) from a GMP-compliant PSC line that is genetically stable and remains so after gene editing and differentiation into islet cells.
   - We have done it in research.

4. Manufacturing enough product to treat the patients that need it.
   - We're working on the challenges of manufacturing at scale

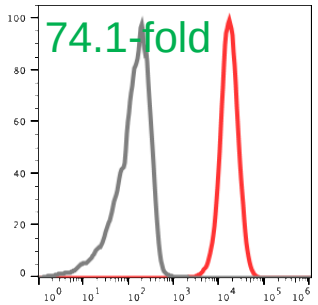
HIP-modification, differentiation and expansion of PSC-derived islet cells



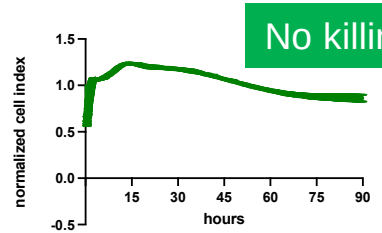
HLA-I



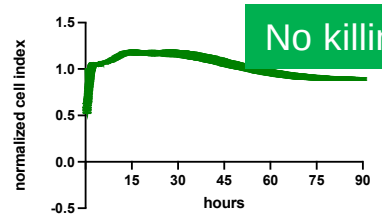
HLA-II



CD47

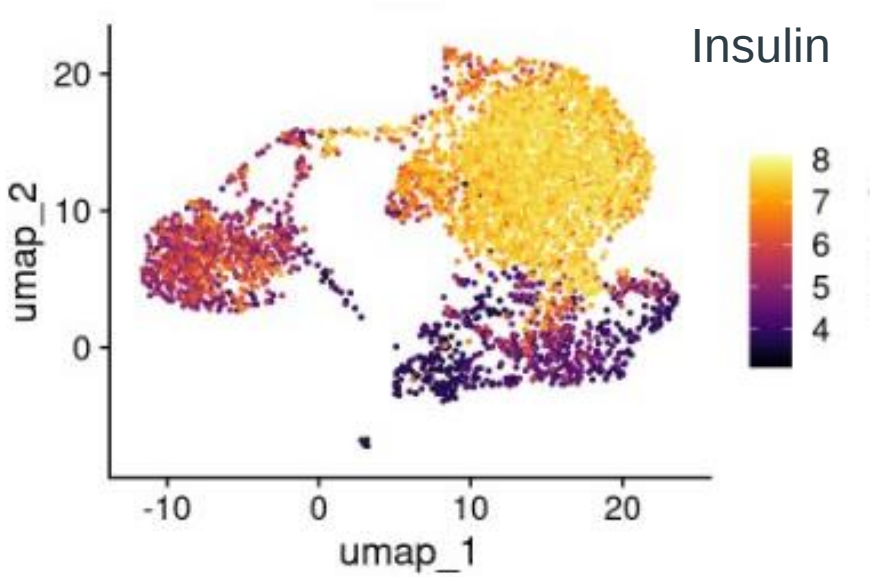


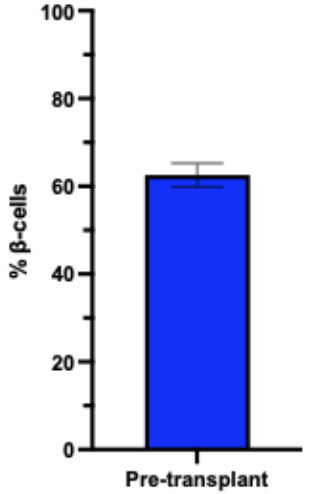
NK-cells

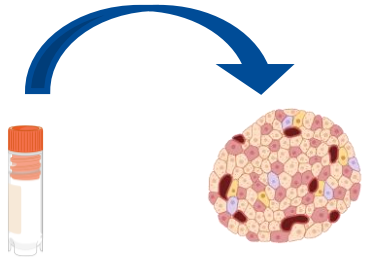


Macrophages

Expected results



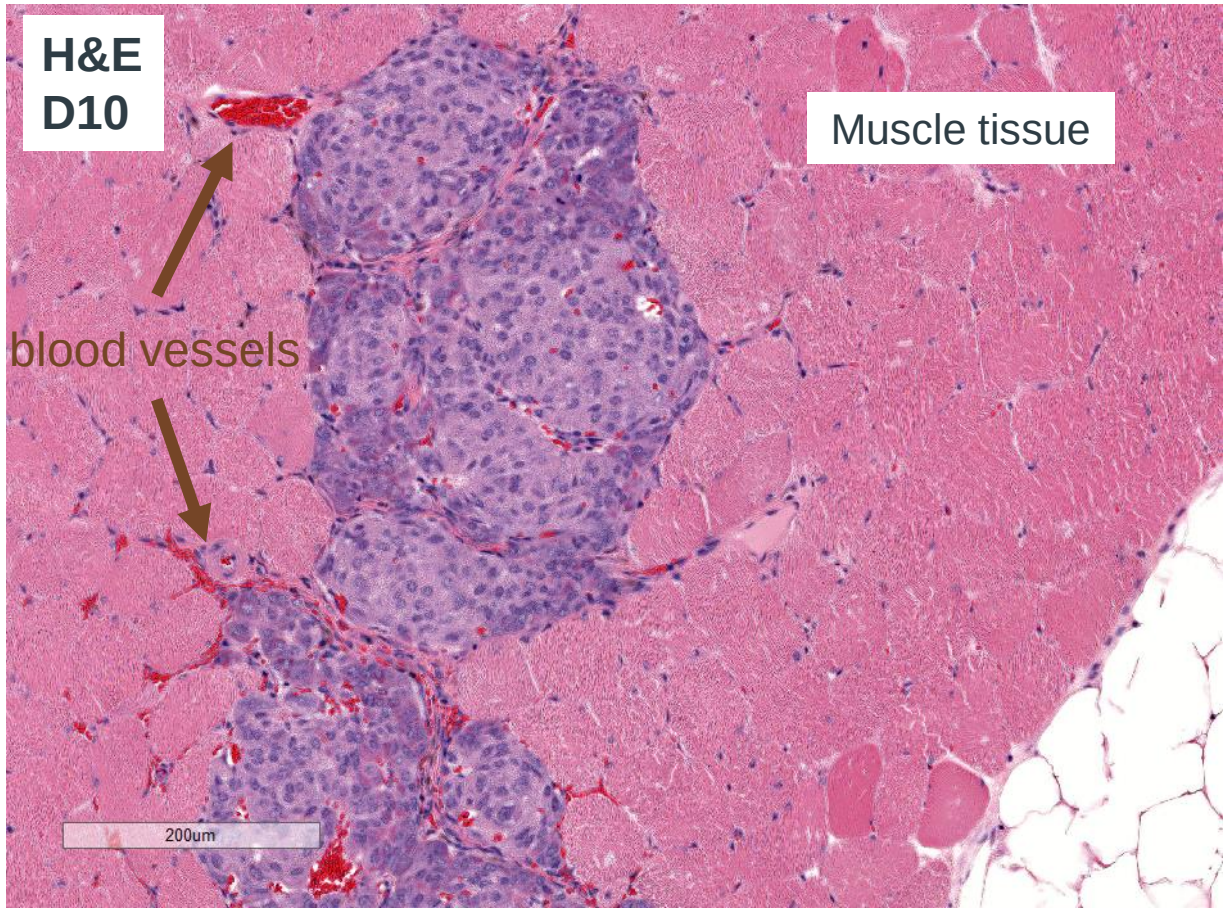


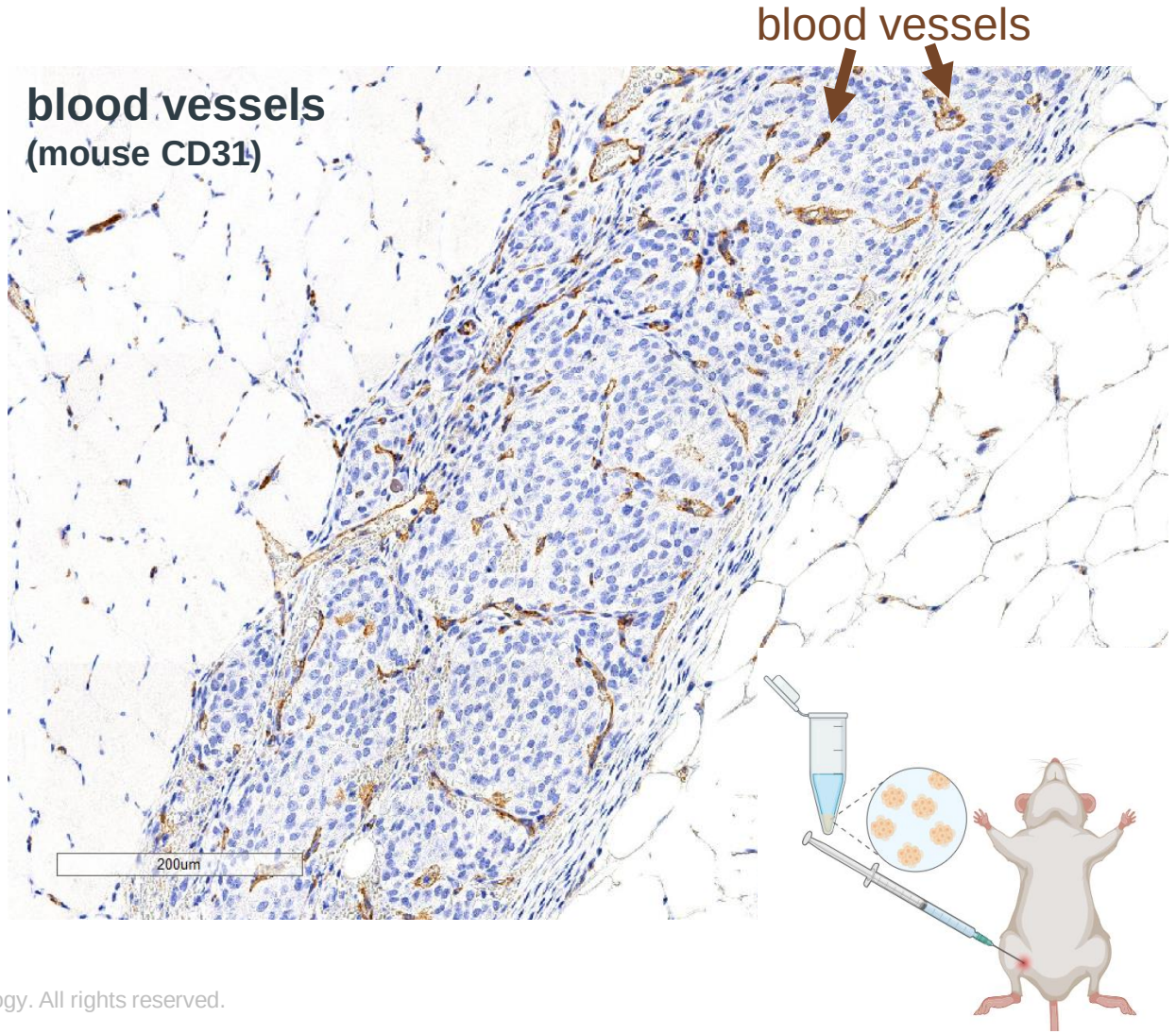


1 Vial of Banked Cells

Yield Billions of Islet Cells

PSC differentiated islet cells transplanted into muscle engraft and are vascularized



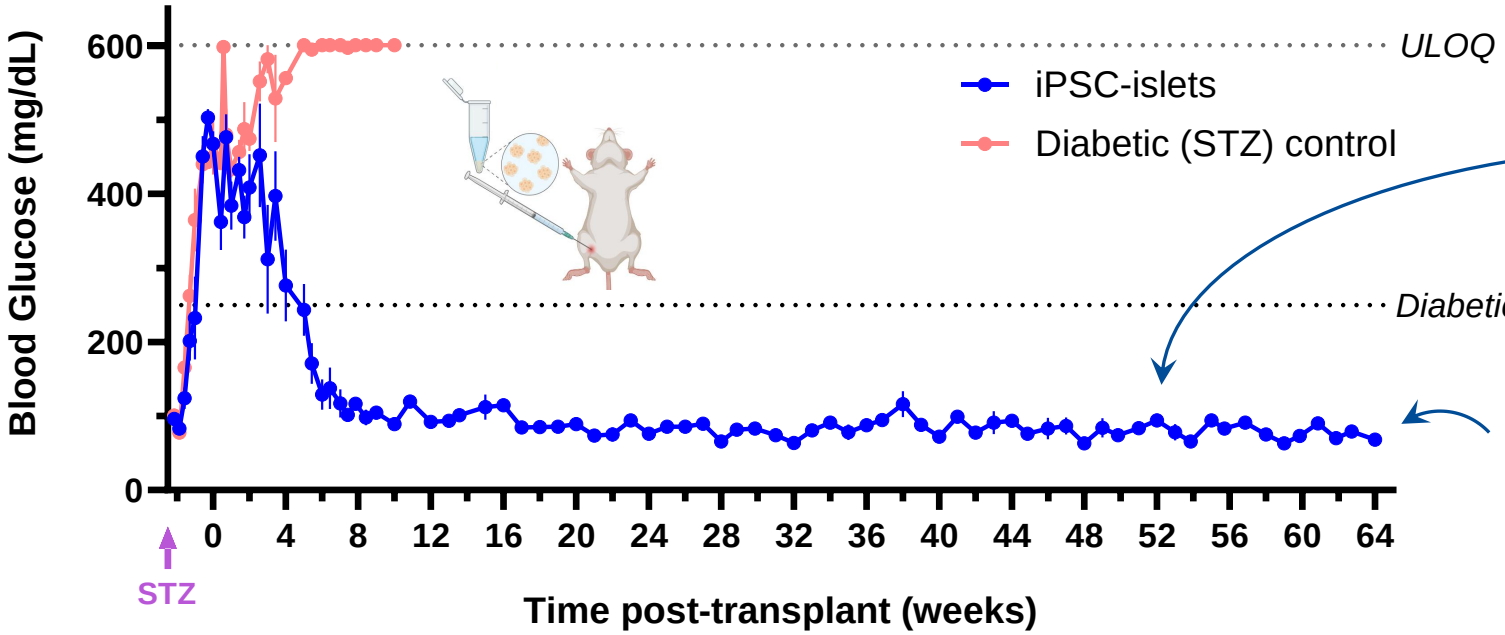


HIP-modified PSC differentiated islet cells transplanted into muscle persist and control blood glucose in mice for >64 weeks

- Maintain normoglycemia (64+ weeks)
- Retain strong expression of hCD47

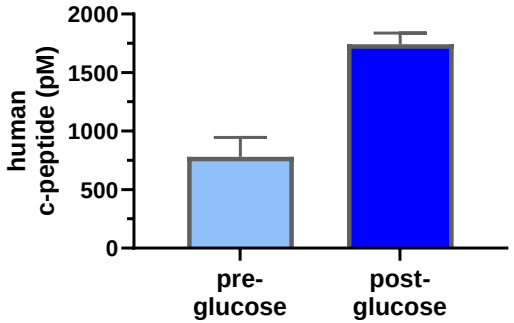
Secrete c-peptide in response to glucose
Densely vascularized

nonfasted blood glucose*

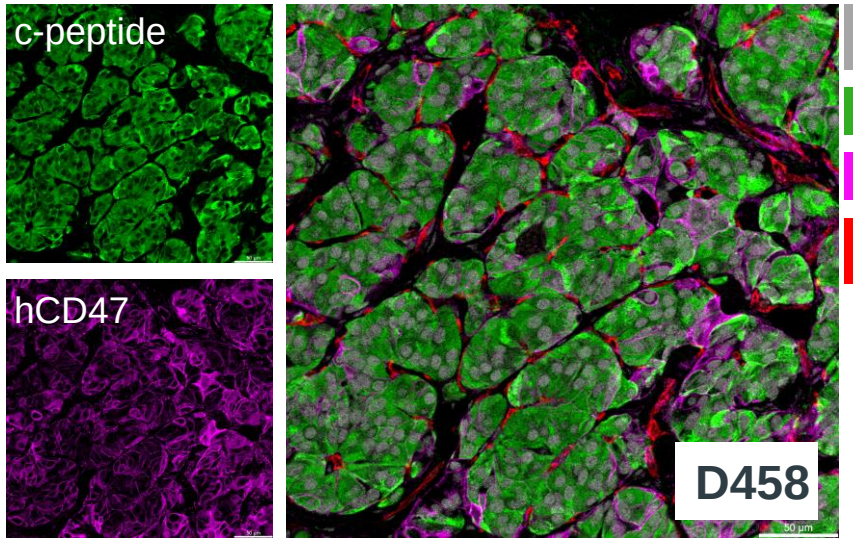


glucose-stimulated human c-peptide**

performed at week 51



graft morphology



*ULOQ: upper limit of quantification; Diabetic threshold at 250 mg/dL; data reported as mean ± S.E.M.
**plasma human c-peptide after 5 hr fast (pre) and 30 min after I.P. 3 g/kg dextrose bolus (post); data is mean ± S.D.

Sana Biotechnology

Clinical Context

Gary Meininger, MD

Sana Biotechnology®

Thank You

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