

SESSION 5

ARE WE THERE YET?

CURRENT STATUS OF THE SEARCH FOR A CURE FOR TYPE 1 DIABETES



Christopher Schaaf
PhD Candidate
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Diabetes



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The logo features the word "EPIC" in large, orange, outlined letters. The letter "C" is replaced by a circular icon containing stylized blue and orange figures of people. Below "EPIC" is the word "DIABETES" in large, bold, black letters, and below that is the word "CONFERENCE" in large, bold, black letters.

EPIC DIABETES CONFERENCE

MAY 3, 2025 CU ANSCHUTZ MEDICAL CAMPUS

EMPOWERING PATIENTS
FOR
INDIVIDUALIZED CARE



LEONARD THOMPSON



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MEANWHILE, IN THE RESEARCH LABS



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A BREAKTHROUGH!



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THE

TORONTO

DAILY

STAR

10TH YEAR.

TWENTY-EIGHT PAGES.

TORONTO, WEDNESDAY, MARCH 22, 1922.

5 O'CLOCK EDITION

TWO CENTS

TORONTO DOCTORS ON TRACK OF DIABETES CURE

RAILROAD UNIONS IN U.S. MAY JOIN IN MINERS' STRIKE

Coal-Diggers Expect Walkout to Be Hundred Per Cent Effective.

PLANS ARE MATURING

President Harding May Make a Public Appeal for Conciliation.

Special to the Star.

Copyright, 1922, by The Associated Press.

WASHINGTON, March 22.—The coal-diggers of the United States are expected to join the miners' strike in a general walkout of the coal industry in the United States, it was learned here today.

The possibility was revealed in the statement, from Washington, that the United States government, in view of the fact that the coal industry is the backbone of the nation's economy, is expected to make a public appeal for conciliation.

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DIABETES SUFFERERS GIVEN MESSAGE OF HOPE

Discovery Made at University of Toronto Will Be Means of Prolonging Life Considerably—E. G. Basing and C. H. Best Probed Experiments All Last Summer.

HANTING STAKES HIS ALL ON THE RESULT

A message of hope to sufferers from diabetes was given yesterday by the medical research department of the University of Toronto.

The discovery was made by E. G. Basing and C. H. Best, who have been working on the problem of diabetes for several years.

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"DRY" LAWS HERE CAUSE HARDSHIP IN OLD FRANCE

French Government Assures New Trade Agreement With Canada

HOME FOR STUDENTS

Opportunity for Our Lads in France

Special to the Star.

Copyright, 1922, by The Associated Press.

PARIS, March 22.—The French government has assured the Canadian government that it is prepared to make a trade agreement with Canada, which would give Canadian students the opportunity to study in France.

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RESERVES OF COAL ARE HIGH IN CITY, PRICE TO GO DOWN

After Strike Trouble Passed Dealer Looks for a Decline

SHUT DOWN IN WEST

Canadian Diggers to Go On Strike With the United States Unions

Special to the Star.

Copyright, 1922, by The Associated Press.

TORONTO, March 22.—The price of coal in this city is expected to decline after the strike in the United States has passed.

The price of coal in this city is expected to decline after the strike in the United States has passed.

CIVIL WAR STAGE NOT YET REACHED, BUT DANGER GREAT

People on Both Sides of Border Apprehend an Attack.

NERVES ALL ON EDGE

No Real Meeting of Troops Yet, But Many Harming Raids.

Imperials May Separate Irish

Special to the Star.

Copyright, 1922, by The Associated Press.

LONDON, March 22.—The British government has announced that it is prepared to make a trade agreement with Ireland, which would give Irish citizens the opportunity to study in Britain.

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DIABETES HAS A TREATMENT

The Nobel Prize in Physiology or Medicine 1923



Photo from the Nobel
Foundation archive.

Frederick Grant
Banting

Prize share: 1/2



Photo from the Nobel
Foundation archive.

John James Rickard
Macleod

Prize share: 1/2

The Nobel Prize in Physiology or Medicine 1923 was awarded jointly to Frederick Grant Banting and John James Rickard Macleod "for the discovery of insulin"



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“Insulin does not belong to me, it belongs to the world” – Frederick Banting



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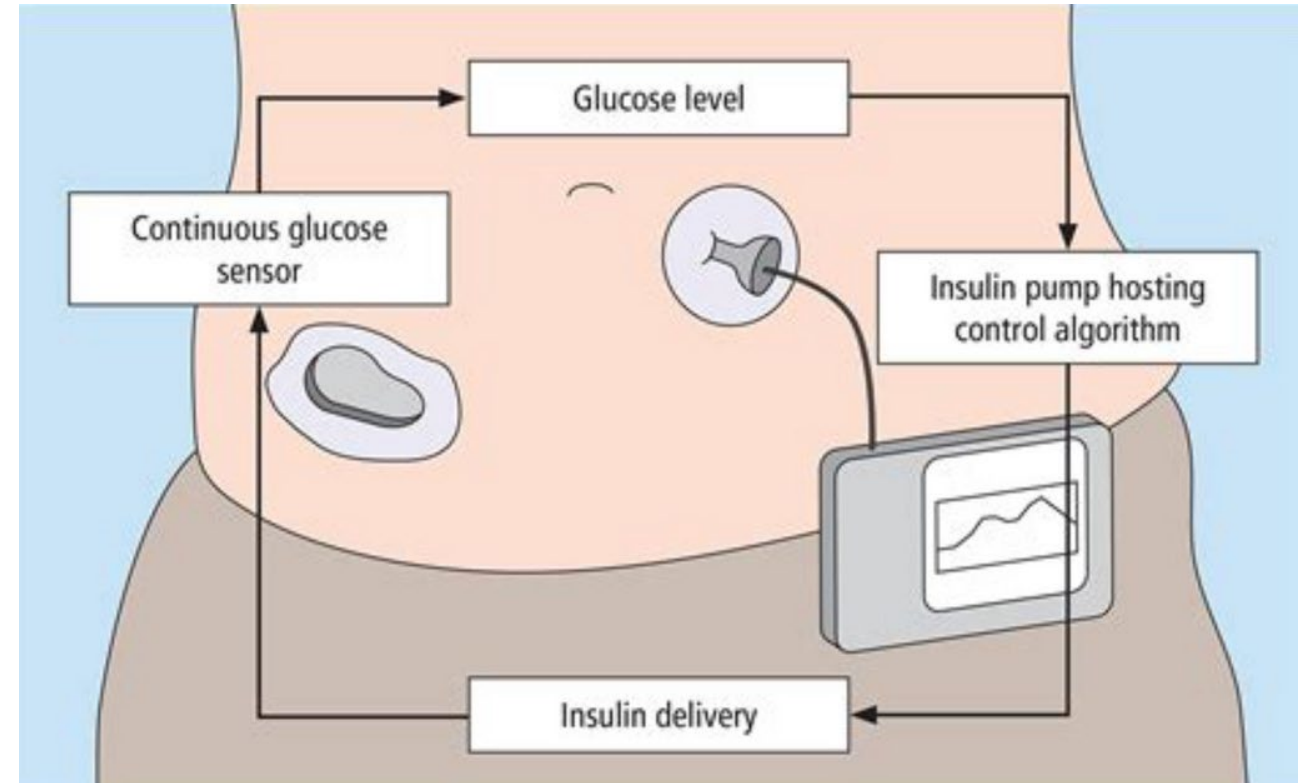
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THE CURRENT STANDARD OF CARE

Hybrid closed-loop insulin pump

- CGM communicates blood glucose level to insulin pump
- Insulin pump adjusts basal rates/delivers correction bolus automatically
- User-initiated mealtime bolus
- Minimal input by patient
- Prone to equipment malfunctions
- Requires multiple devices to be worn on body



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WHERE DO WE GO FROM HERE?

Prevention

- Delaying or stopping onset of the disease



- Effective in Stage 2 diabetes
 - “honeymoon period”
 - Delays onset by an average of 2 years

Functional cure

- Islet transplants
 - Transplant of donor tissue into a patient to replace the lost beta-cells
- Cell therapies
 - Generate new insulin-producing beta cells to transplant into a patient

Goal: to *functionally* cure T1D. Remove any need for exogenous insulin administration (injections/pump infusion) or blood glucose monitoring.

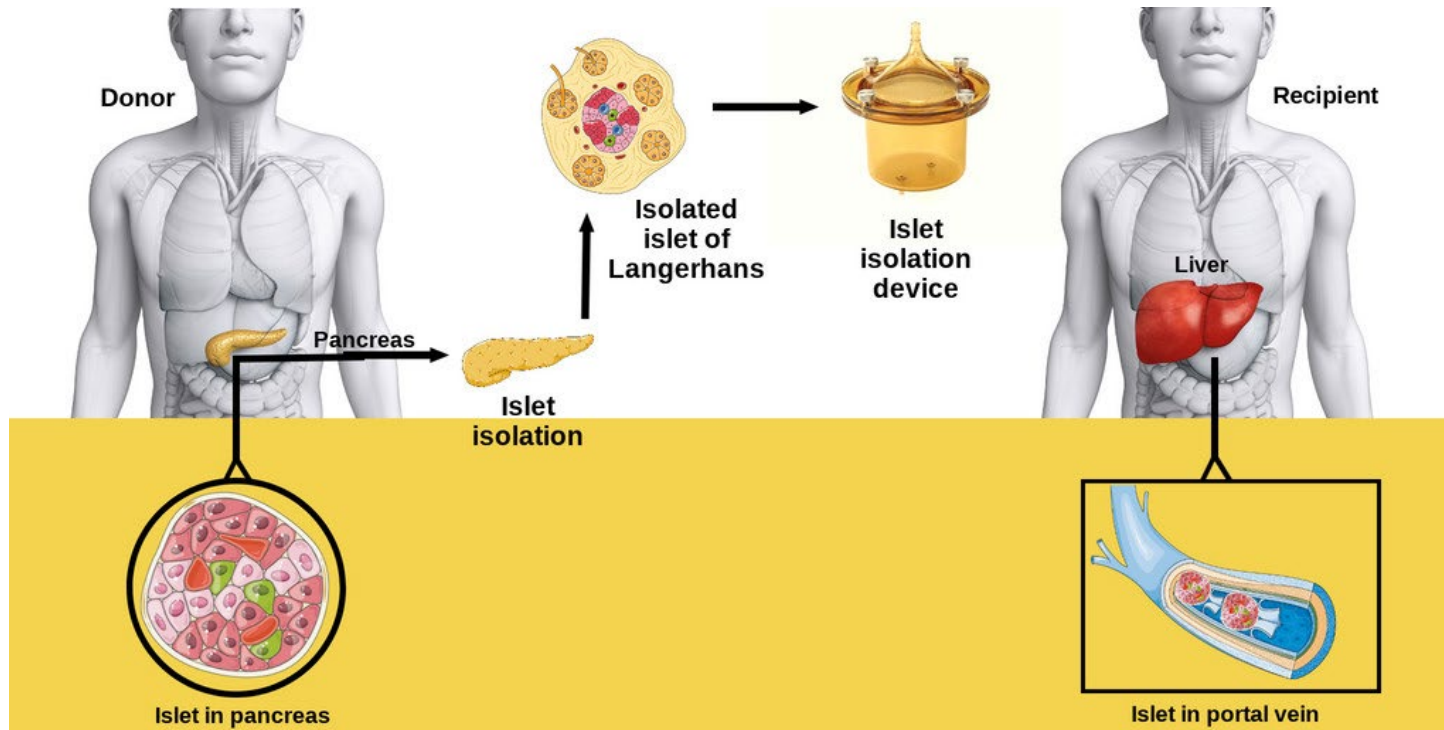


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ISLET TRANSPLANTS



The Edmonton Protocol (1999)

- Acquires cadaveric islets from donor
- Islets are isolated from donor pancreas
- Whole Islets are transplanted into recipient hepatic portal vein
- Requires immunosuppressive regimen
- Requires cadaveric donor tissue
 - *Massive barrier to its use as a widespread treatment*

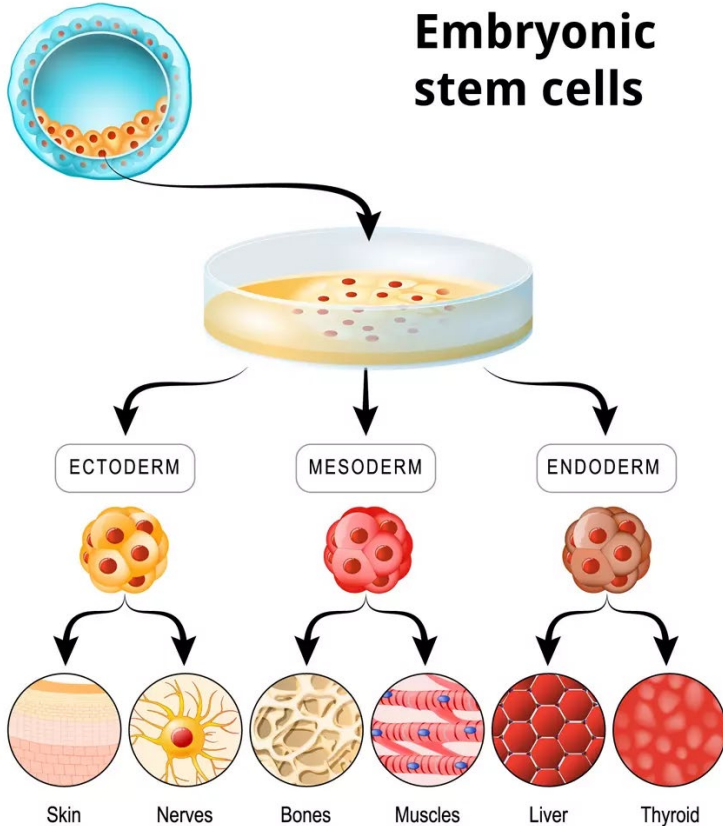


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STEM CELLS AS A SOURCE OF BETA CELLS



Stem cells

- *Pluripotency* – ability to become most cell types in the body
- Provide an “unlimited” source of beta cells
 - Can be expanded indefinitely in the lab

Can be differentiated into insulin-producing beta cells

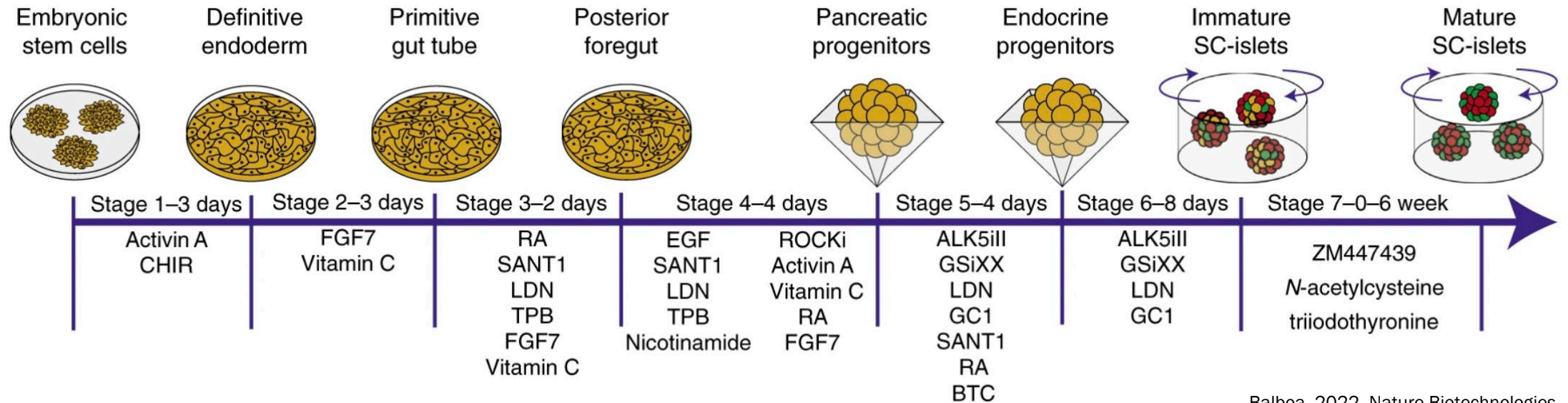


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BETA CELL DIFFERENTIATION PROTOCOLS



Balboa, 2022, Nature Biotechnologies



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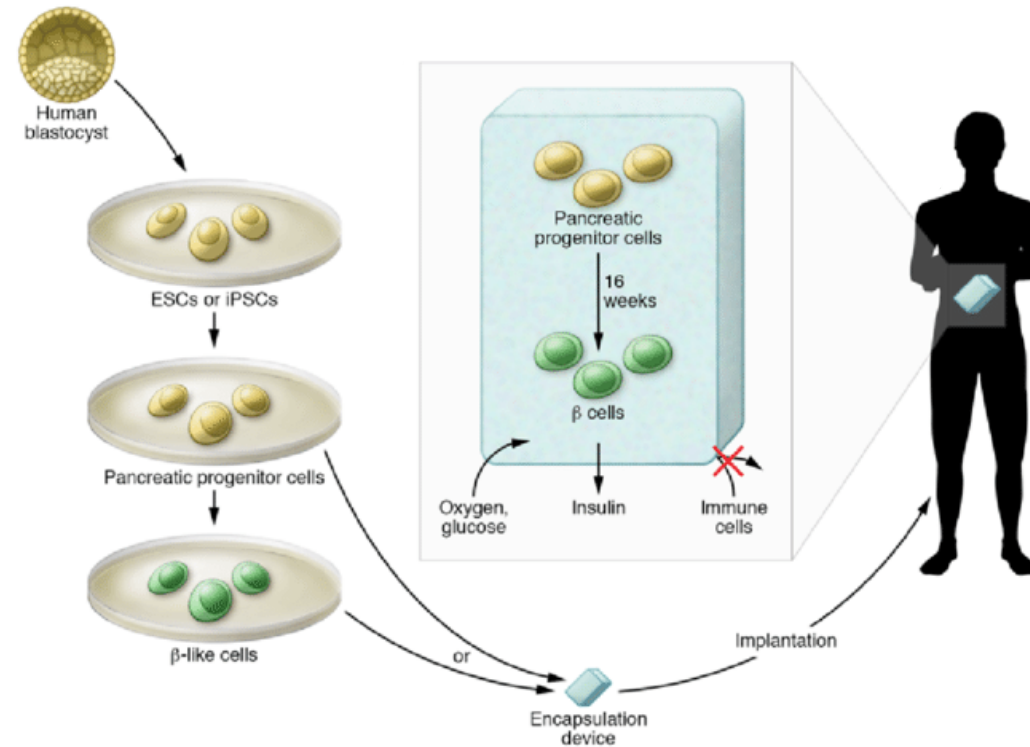
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STEM CELL THERAPIES TO TREAT DIABETES

Stem cell therapies

- Stem cells maintained in the lab
- Differentiated into beta cells
- Implanted into patient
- Restore insulin production to the patient, without the need for insulin injections/infusions



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A BREAKTHROUGH?

The New York Times

A Cure for Type 1 Diabetes? For One Man, It Seems to Have Worked.

A new treatment using stem cells that produce insulin has surprised experts and given them hope for the 1.5 million Americans living with the disease.

Stem cell derived beta cell transplant, *in combination with immunosuppression*

- Still required exogenous insulin administration daily, and maintained diabetic HbA1C levels, albeit reduced. Other studies have shown better results.



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THE IMMUNE SYSTEM



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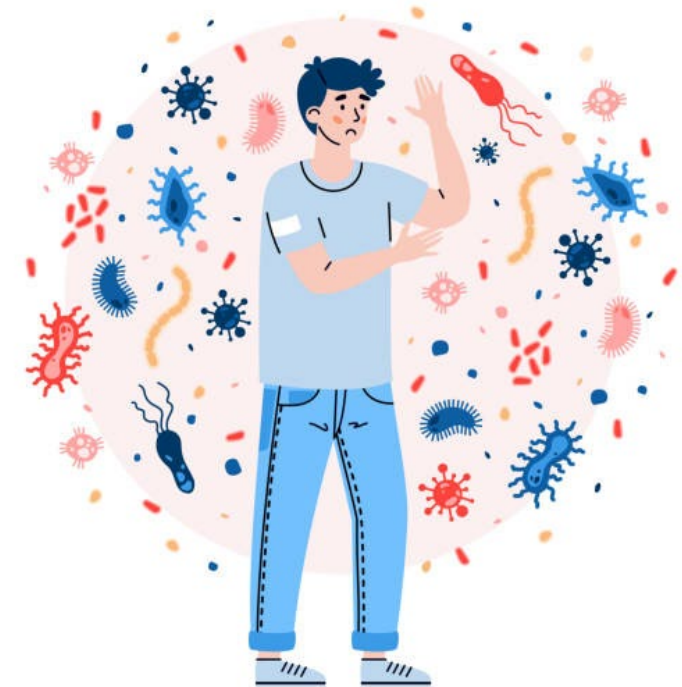
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IMMUNOSUPPRESSANTS

Immunosuppressive regimens

- Lower the immune systems function
- Allows for acceptance of the graft/transplant
 - Medium term (1-3 years)
- Weakened immune system and long-term complications
 - Kidney toxicity
 - High blood pressure
 - Nervous system toxicity
 - Decreased bone marrow
 - Liver toxicity
 - Osteoporosis
 - Flu-like symptoms
 - Nervous system dysregulation



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A NEW SOURCE OF STEM CELLS

The Nobel Prize in Physiology or Medicine 2012

The Nobel Prize in Physiology or Medicine 2012 was awarded jointly to Sir John B. Gurdon and Shinya Yamanaka "for the discovery that mature cells can be reprogrammed to become pluripotent"



© The Nobel Foundation. Photo:
U. Montan
Sir John B. Gurdon
Prize share: 1/2



© The Nobel Foundation. Photo:
U. Montan
Shinya Yamanaka
Prize share: 1/2



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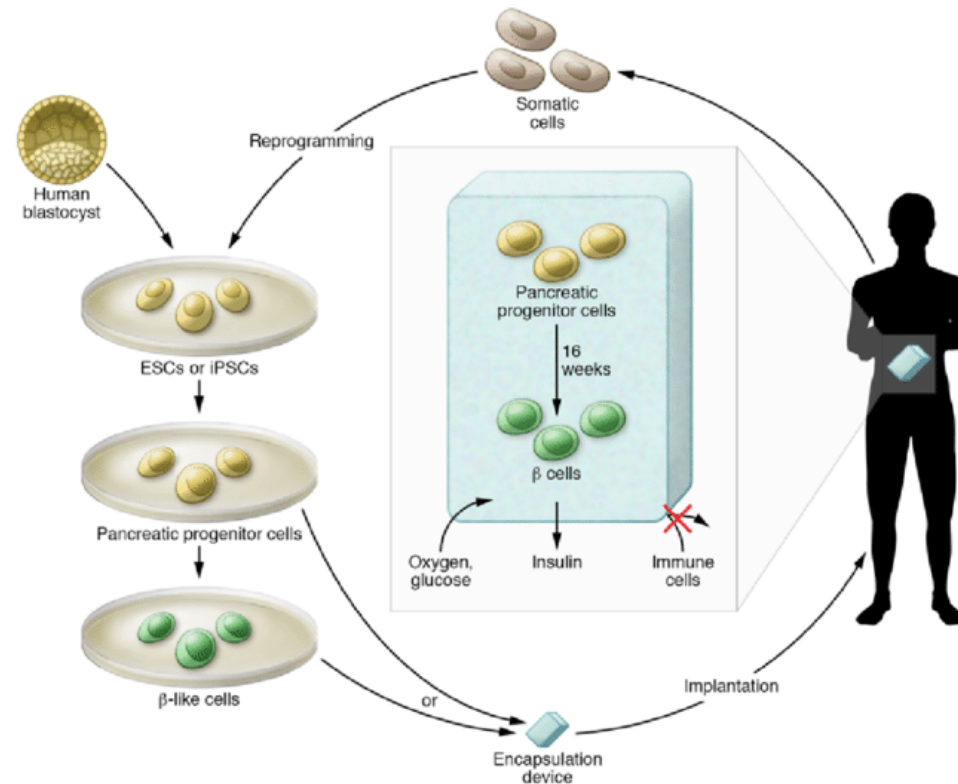
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REPLACEMENT THERAPY FROM THE PATIENT'S OWN CELLS

Induced pluripotent stem cell-derived beta cell transplant is an autologous treatment

- Does not invoke an immune response for host vs graft
- Stem cells provide an “unlimited” source of cells, no donor needed

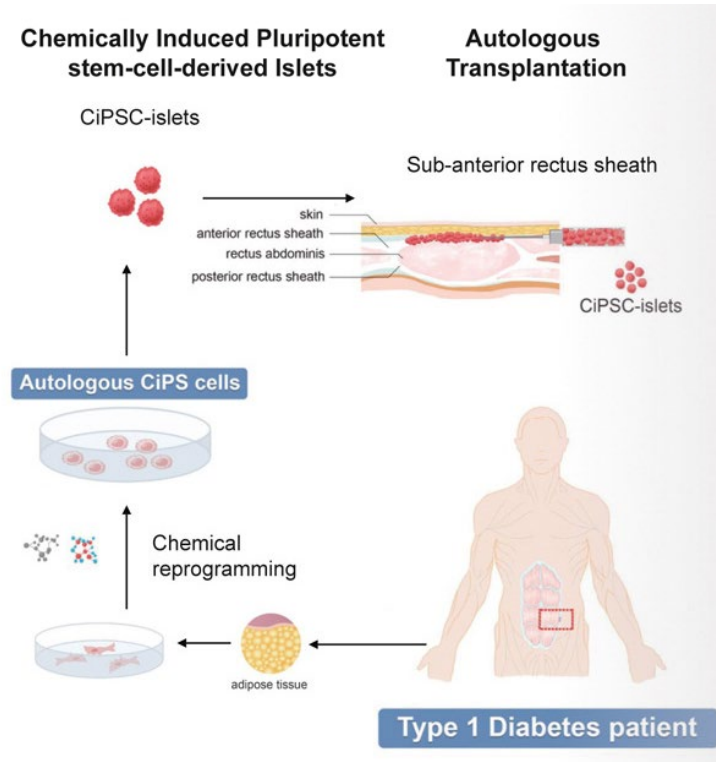


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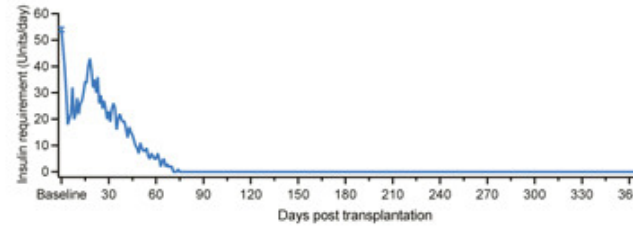


INDUCED PLURIPOTENT STEM CELL-DERIVED BETA CELLS

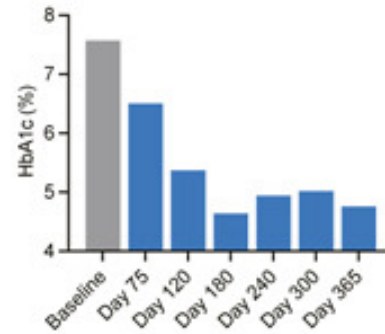


Wang, et al. 25 September 2024, Cell

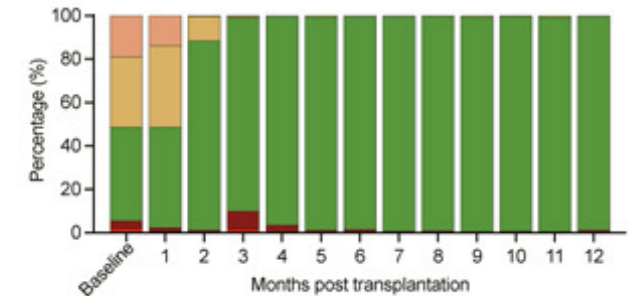
Insulin independence from 75 days post-transplantation



Decrease in glycated hemoglobin



Time-in-target glycemic range > 98%



Patient had received two prior liver transplants, and a whole pancreas transplant.

Pancreas graft was removed one year later due to complications.

Patient was on, and remained on **immunosuppression** for the duration of the study.



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Source of tissue	Outcome	Barriers
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Type 1 diabetes is an autoimmune condition. We need to not only prevent rejection of the transplant, but also the **autoimmune response** from attacking the newly transplanted tissue



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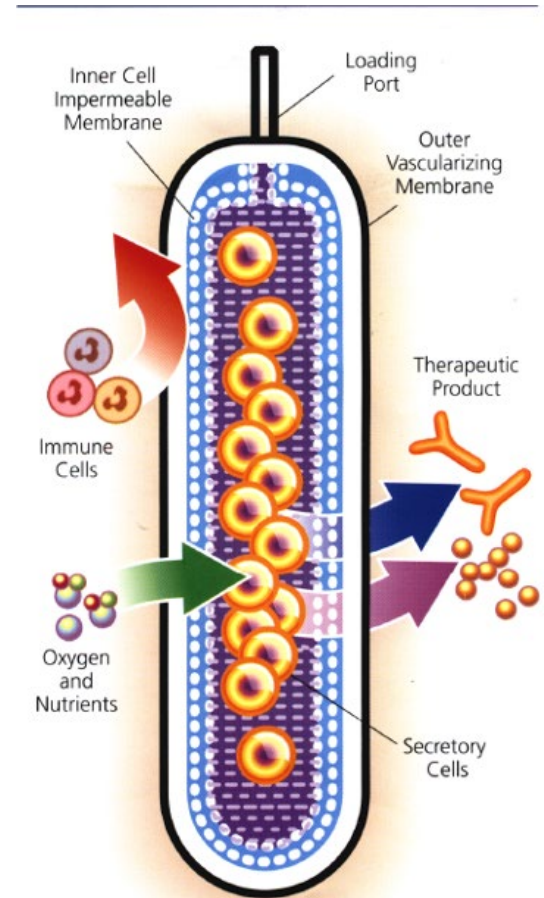
IMMUNOISOLATION DEVICES

Allow for protection of implanted cells from the immune system

- Prevents host graft rejection
 - Allows for allogeneic therapy
- Prevents the autoimmune response from killing the implanted cells

Historically, devices are highly susceptible to fibrotic overgrowth, and a lack of oxygen availability for cells

New clinical trials are underway, with patients already enrolled and dosed



Immunoisolation concept of the TheraCyte® System



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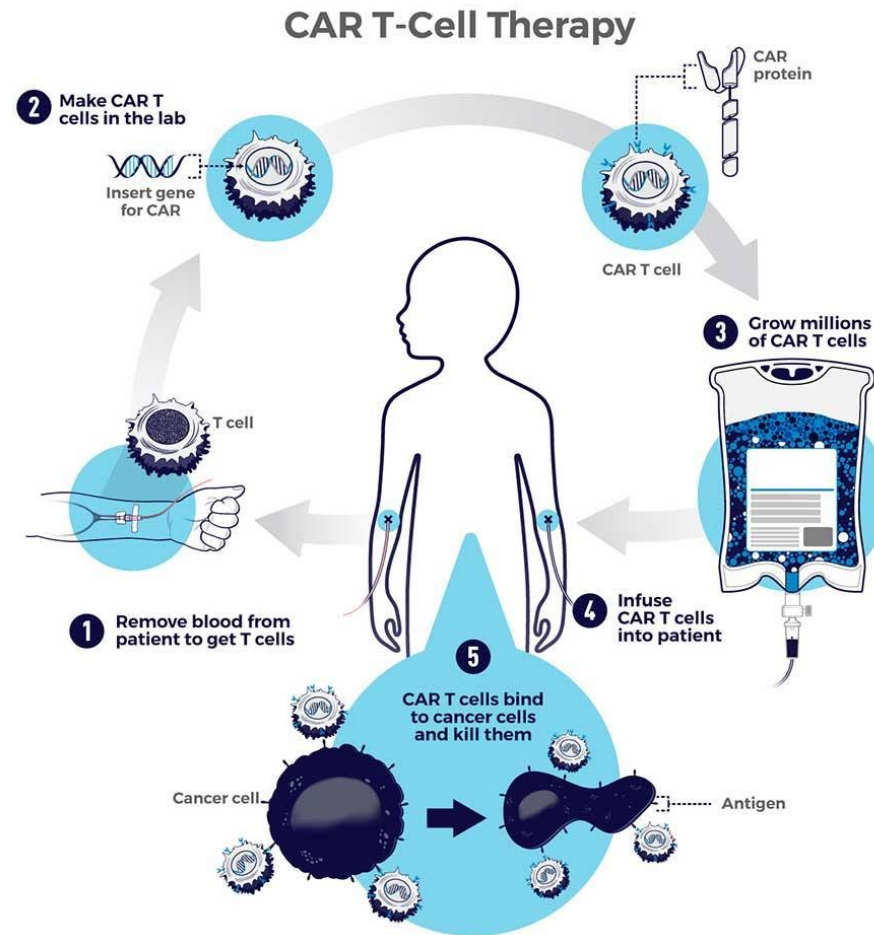


EDITING THE GENOME

Cells are taken from the body,
genetically edited in the lab,
and returned into the patient.

This is already being done with
cancer treatments!

What if we take a similar
approach to stem cell derived
beta cells? Can we genetically
edit cells to evade the immune
system?



cancer.gov



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IMMUNNE-PRIVILEGED STEM CELL DERIVED BETA CELLS



First-in-human Safety Study of Hypoimmune Pancreatic Islet Transplantation in Adult Subjects With Type 1 Diabetes

ClinicalTrials.gov ID [NCT06239636](#)

Sponsor [Per-Ola Carlsson](#)

Information provided by [Per-Ola Carlsson, Uppsala University Hospital \(Responsible Party\)](#)

Last Update Posted [2024-12-11](#)

Sana Biotechnology Announces Positive Clinical Results from Type 1 Diabetes Study of Islet Cell Transplantation Without Immunosuppression

January 7, 2025

Cells are alive, functional, and tolerated after
28 days

with no immunosuppression



An Open-Label, FIH Study Evaluating the Safety, Tolerability, and Efficacy of VCTX211 Combination Product in Subjects With T1D

ClinicalTrials.gov ID [NCT05565248](#)

Sponsor [CRISPR Therapeutics AG](#)

Information provided by [CRISPR Therapeutics \(CRISPR Therapeutics AG\) \(Responsible Party\)](#)

About VCTX211

VCTX211 is an **allogeneic, gene-edited, stem cell-derived** investigational therapy for the treatment of T1D, which incorporates additional gene edits that aim to further enhance cell fitness. This immune-evasive cell replacement therapy is designed to enable patients to produce their own insulin in response to glucose.



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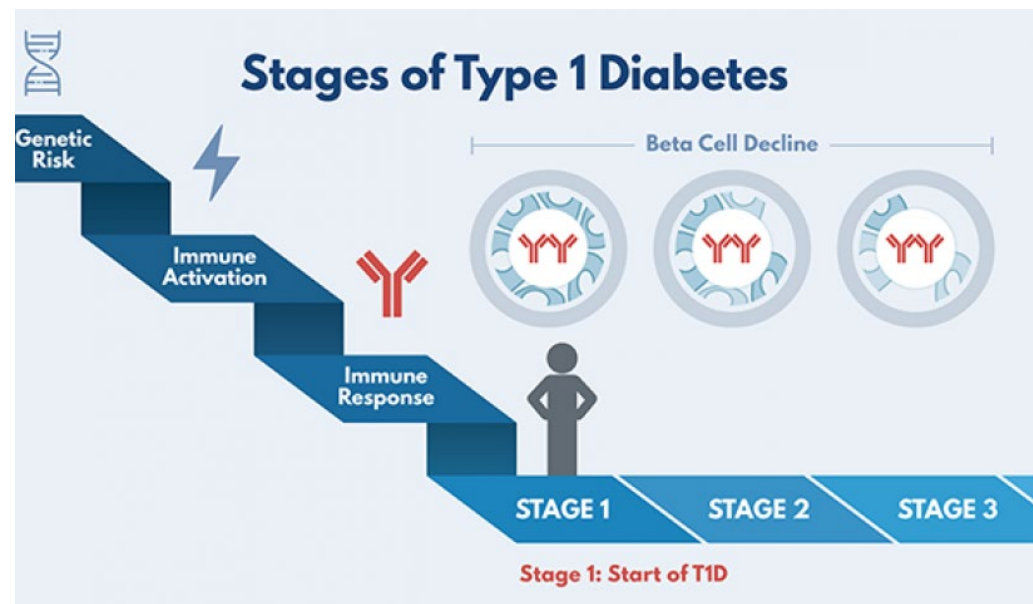
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1922



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“Insulin does not belong to me, it belongs to the world” –Sir Frederick Banting, 1922



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