# SESSION 1

# PREVENTION AND DELAY OF TYPE 1 DIABETES. TO WHOM AND WHEN?


Aaron Michels, MD
Professor of Pediatrics, Medicine, and Immunology
Frieda and George S. Eisenbarth Clinical Immunology Endowed Chair
Barbara Davis Center for Diabetes
University of Colorado Anschutz Medical Campus

Kimber Simmons, MD, MS
Associate Professor of Pediatrics
Barbara Davis Center for Diabetes
University of Colorado Anschutz Medical Campus


Barbara Davis Center for Diabetes • Children's Diabetes Foundation •

#EPICconf2024

www.EPICconferences.org

EMPOWERING PATIENTS FOR INDIVIDUALIZED CARE
EPIC
DIABETES CONFERENCE

# EPIC DIABETES CONFERENCE

JUNE 1, 2024, CU ANSCHUTZ MEDICAL CAMPUS

## EMPOWERING PATIENTS FOR INDIVIDUALIZED CARE

Barbara Davis Center for Diabetes • Children's Diabetes Foundation •

# COI

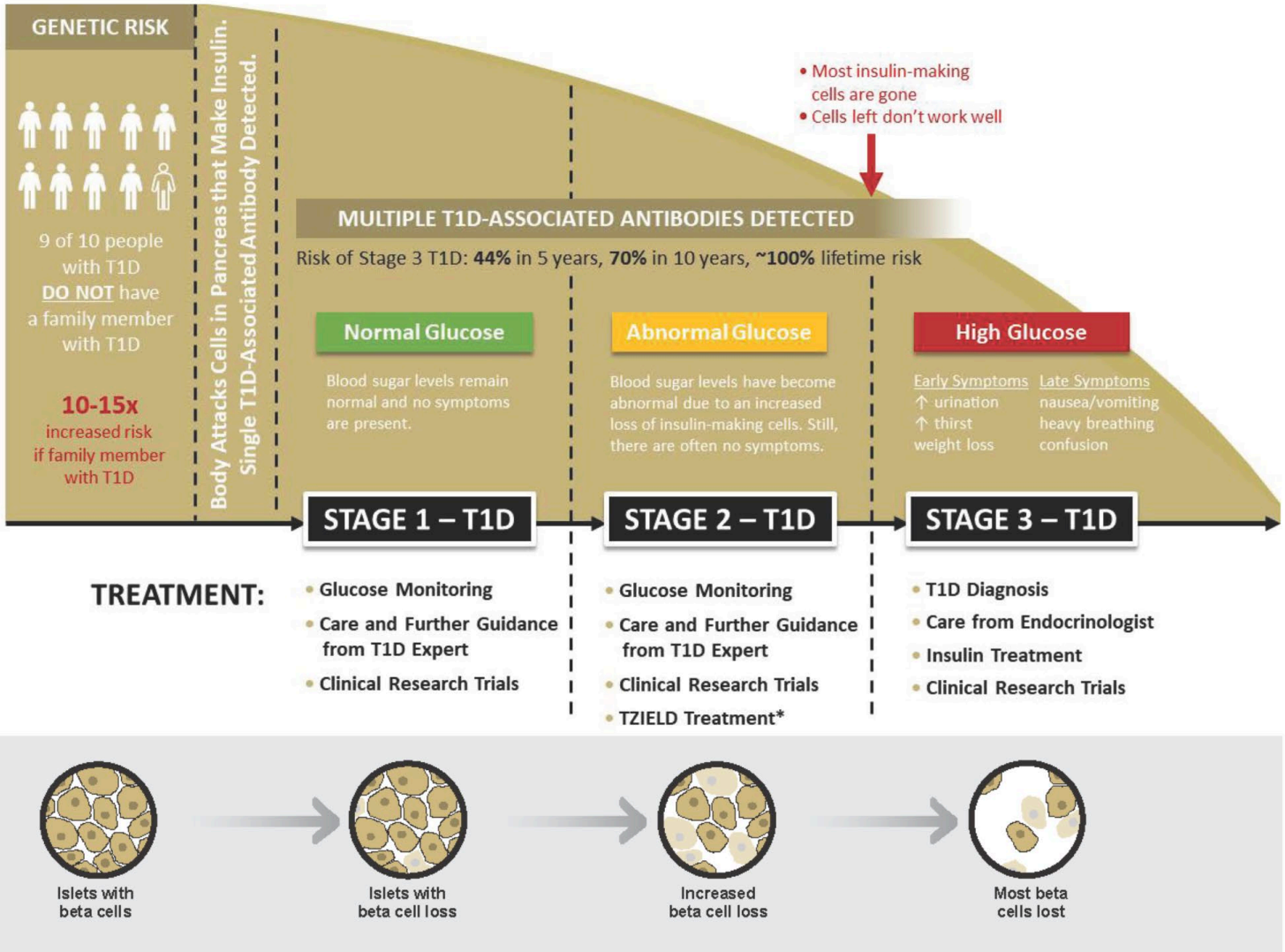
Michels

- Research grant funding from the National Institutes of Health (NIH), Helmsley Charitable Trust (HCT), and Juvenile Diabetes Research Foundation (JDRF)
- Scientific founder and shareholder in ImmunoMolecular Therapeutics, biotech company

Simmons

- Research grant funding from the National Institutes of Health (NIH/NIDDK), Juvenile Diabetes Research Foundation (JDRF), Helmsley Charitable Trust (HCT), Provention Bio, Sanofi, Novartis
- Advisory board member for Sanofi, Provention Bio, Shoreline Biosciences
- Board of directors for Diabetes Training Camp
- Honorarium: Medscape, Med Learning Group

# TYPE 1 DIABETES CAN BE DIAGNOSED WHEN BLOOD SUGARS ARE NORMAL AND INSULIN IS NOT YET NEEDED




* TZIELD Treatment: Potential eligible patients are those who are 8 years or older with stage 2 T1D

FDA NEWS RELEASE

# FDA Approves First Drug That Can Delay Onset of Type 1 Diabetes



**For Immediate Release:** November 17, 2022

Today, the U.S. Food and Drug Administration approved Tzield (teplizumab-mzwv) injection to delay the onset of stage 3 type 1 diabetes in adults and pediatric patients 8 years and older who currently have stage 2 type 1 diabetes.

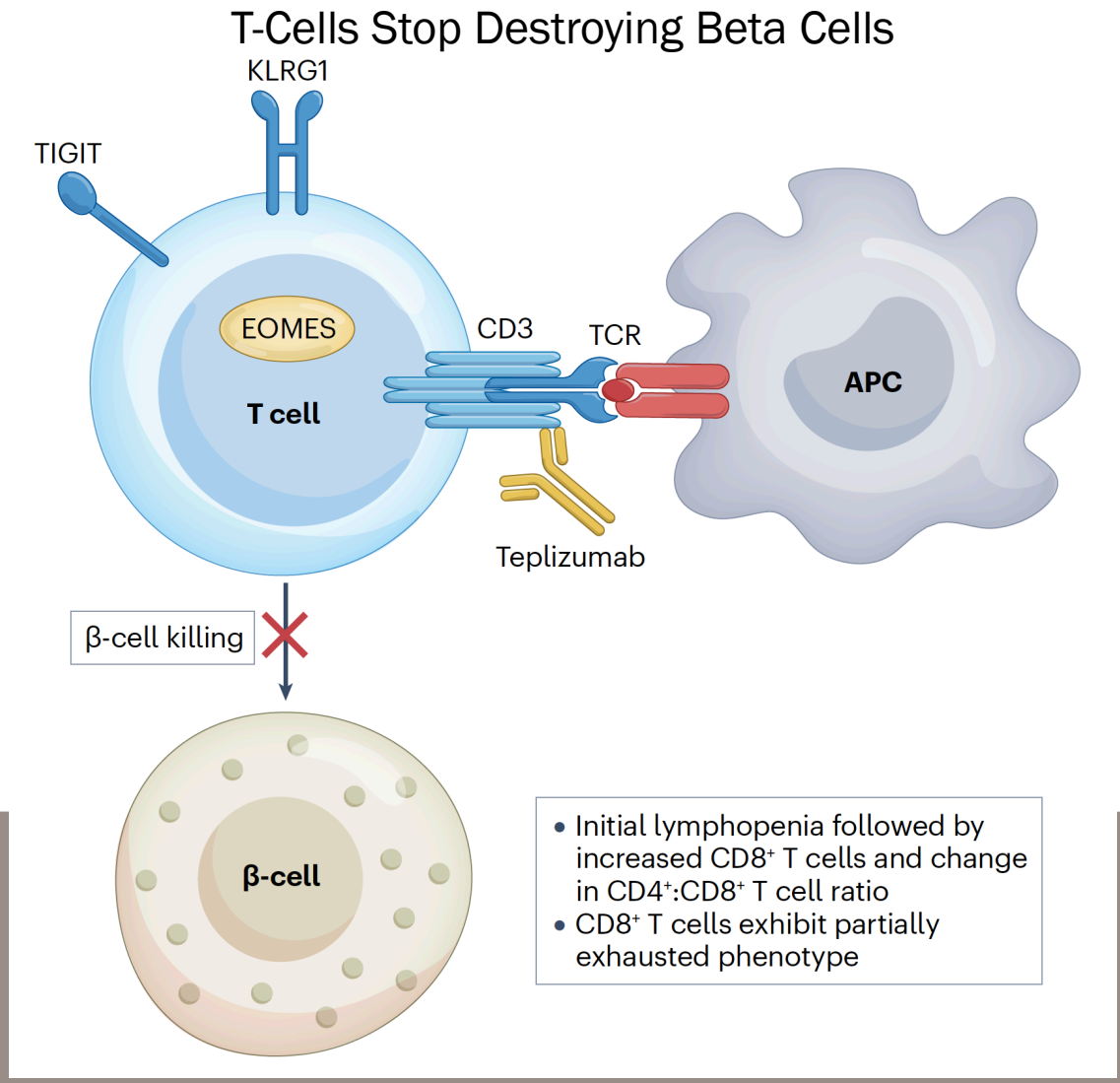
**"Today's approval of a first-in-class therapy adds an important new treatment option for certain at-risk patients," said John Sharretts, M.D., director of the Division of Diabetes, Lipid Disorders, and Obesity in the FDA's Center for Drug Evaluation and Research. "The drug's potential to delay clinical diagnosis of type 1 diabetes may provide patients with months to years**

**Content current as of:**
11/17/2022

**Regulated Product(s)**
Drugs

# WHAT IS TEPLIZUMAB?

- Given for 30 minutes a day for 14 days in a row through an intravenous catheter
- Requires monitoring post infusion and some lab tests to check for drug infusion reactions and cytokine release syndrome



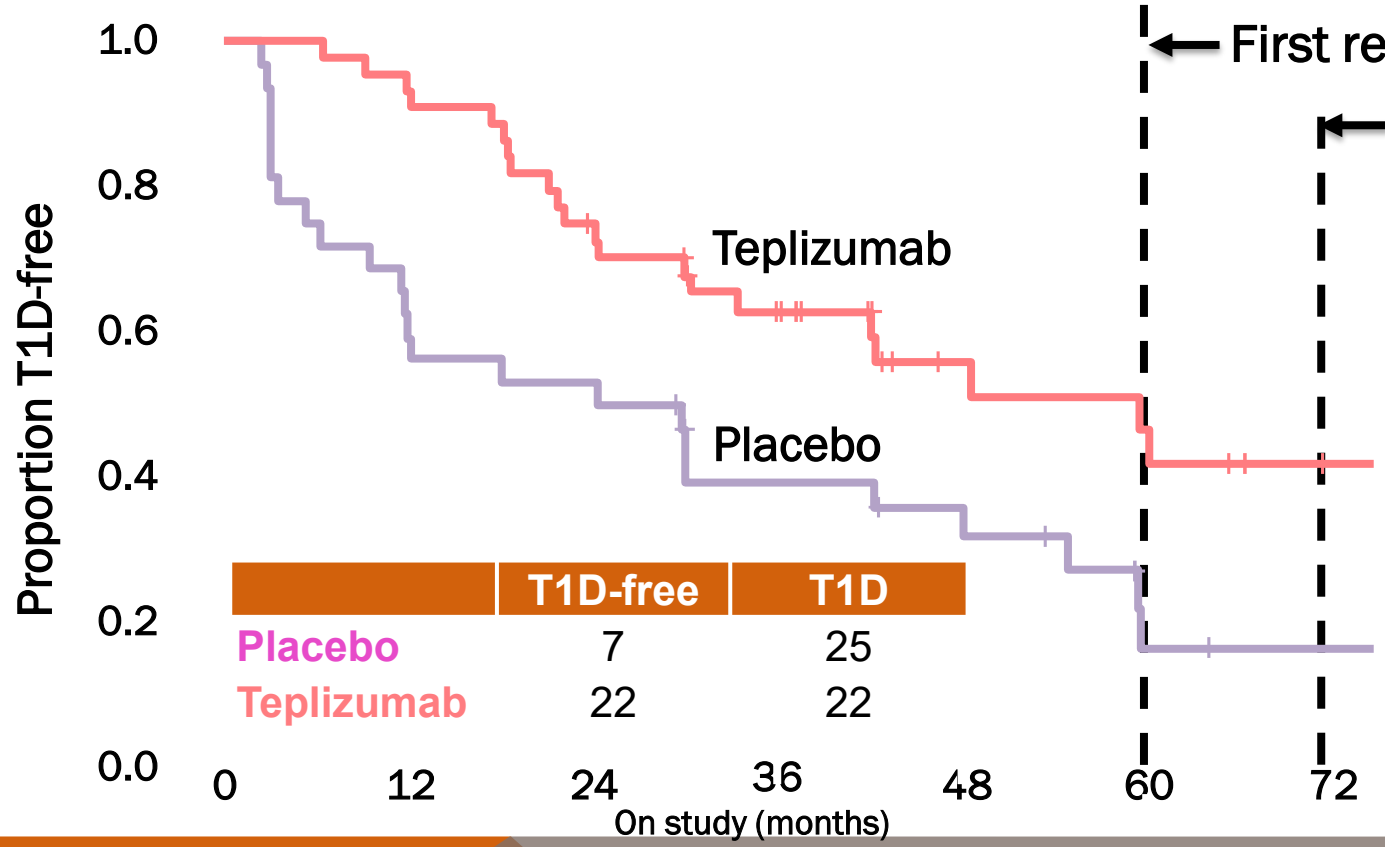

Herold KC, et al. *Nature Reviews Immunoloty.* 2024.

# TEPLIZUMAB CAN BE GIVEN TO PEOPLE WITH STAGE 2 TYPE 1 DIABETES

- Blood test to screen for type 1 diabetes associated (islet) autoantibodies is positive (autoimmune type 1 diabetes)
- Age 8 years are older
- Blood glucoses are abnormal but have never been high enough for diagnosis
  - 2-hour oral glucose tolerance test glucose 140-199 mg/dl
  - HbA1c 5.7-6.4%
  - Fasting glucose 100-125 mg/dl

**Teplizumab can be prescribed to delay the onset of type 1 diabetes**

# TEPLIZUMAB DELAYS THE ONSET OF TYPE 1 DIABETES




5 years after treatment, the median delay to stage 3 was 2 years with teplizumab

6 years after treatment, the median delay to stage 3 was 33 months with teplizumab

By 6 years only 50% of teplizumab-treated patients developed stage 3 T1D compared to 78% in the placebo group

| Number at risk | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Placebo | 32 | 24 | 19 | 18 | 17 | 14 | 11 | 11 | 9 | 7 | 3 | 2 | 0 |
| Teplizumab | 44 | 44 | 41 | 39 | 32 | 29 | 23 | 19 | 12 | 11 | 10 | 8 | 0 |

Herold KC, et al. *N Engl J Med.* 2019;381:603-613. Sims EK, et al. *Sci Transl Med.* 2021:13(583):eabc8980.

# What would 2 or more years without type 1 diabetes mean to you and/or your family?

4,380 to 7,300 finger pokes
80 CGM sensor insertions
2,920 insulin injections
300 infusion set changes

# TEPLIZUMAB HAS PRESERVED INSULIN-PRODUCING BETA CELLS IN NEW ONSET TRIALS OVER THE LAST 20 YEARS

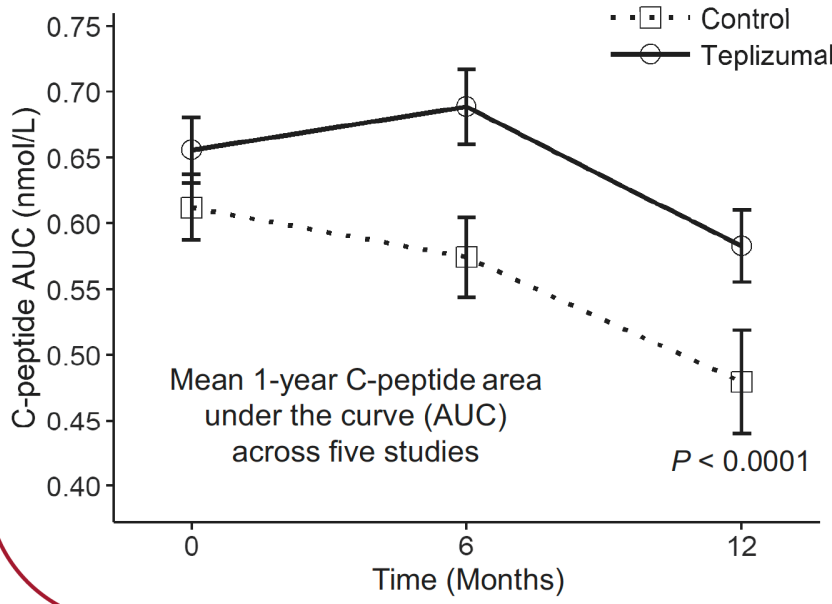
**Five clinical trials**

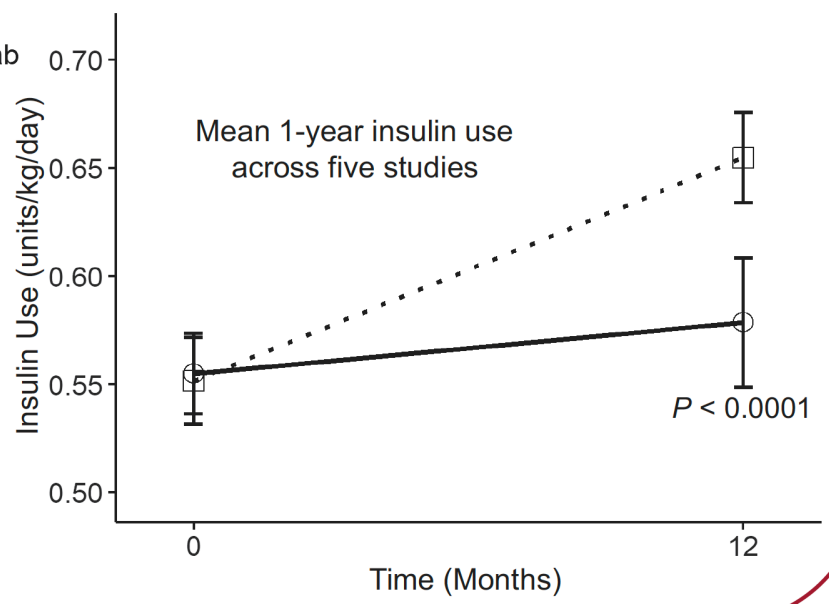
**Stage 3 type 1 diabetes**

| Teplizumab | Control |
|---|---|
| n=375 | n=234 |


## *Key Result*

**Stimulated C-peptide and insulin use were significantly improved in Stage 3 type 1 diabetes participants treated with teplizumab**

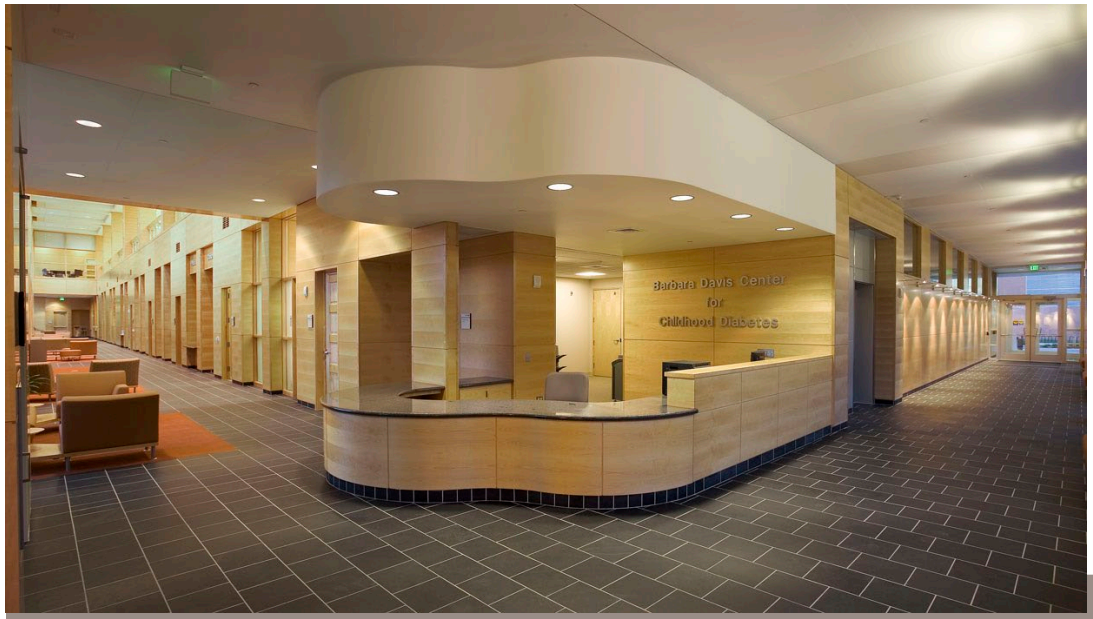



Herold KC, et al. *Diabetes Care.* 2023;46(10):1848-1856.

# BDC EARLY STAGE TYPE 1 DIABETES CLINICAL EXPERIENCE

- Opened Early T1D Clinic 12/9/2022
- 63 clinical visits for multiple T1D-related autoantibody-positive individuals with concern for dysglycemia as of 4/1/2024
- 42 patients completed full metabolic staging
  - 23 children (ages 8-17 years)
  - 6 young adults (ages 18-26 years)
  - 13 adults (ages 28-62 years)



# BDC INFUSION EXPERIENCE

**Opened Infusion Center 4/10/2023**

**16 individuals treated with teplizumab as of 4/1/2024**

| | |
|---|---|
| Age: | Mean 18.1±7.9 years, range 10-40 years |
| | 56% <18 years, 25% 18-26 years, |
| | 19%>26 years |
| Sex: | 56% female, 44% male |
| Race: | 75% (n=12) White, 19% (n=3) Hispanic, |
| | 6% (n=1) Asian |

# SIDE EFFECTS

| Teplizumab Side Effects | Clinical Trials % (N=791) | BDC Clinical Experience % (N=16) |
|---|---|---|
| **Lymphopenia** | **79.9% (632)** | **100% (16)** |
| **Leukopenia** | **63.3% (501)** | **81.3% (13)** |
| Neutropenia | 39.6% (313) | 43.8% (7) |
| **Rash** | 34.5% (273) | **81.3% (13)** |
| Anemia | 28.8% (228) | 6.3% (1) |
| **AST increased** | 28.1% (222) | **50% (8)** |
| **Headache** | 27.2% (215) | **56% (9)** |
| ALT increased | 26.5% (210) | 43.8% (7) |
| Thrombocytopenia | 21.7% (172) | 12.5% (2) |
| **Nausea** | **19.6% (155)** | **87.5% (14)** |
| Cytokine Release Syndrome (CRS) | 5.8% (4) | 12.5% (2) |

Herold K et al., *Diabetes* Care, 2023; BDC clinic

1. Get screened for type 1 diabetes with a blood test to measure the four type 1 diabetes autoantibodies.
2. If positive, determine stage of type 1 diabetes with a clinic or research team.
3. If stage 2 type 1 diabetes consider a research trial or clinical treatment with teplizumab.

If you wait for symptoms of diabetes to develop, then you are too late for treatment to delay or research to prevent type 1 diabetes.

# TYPE 1 DIABETES IN 2024

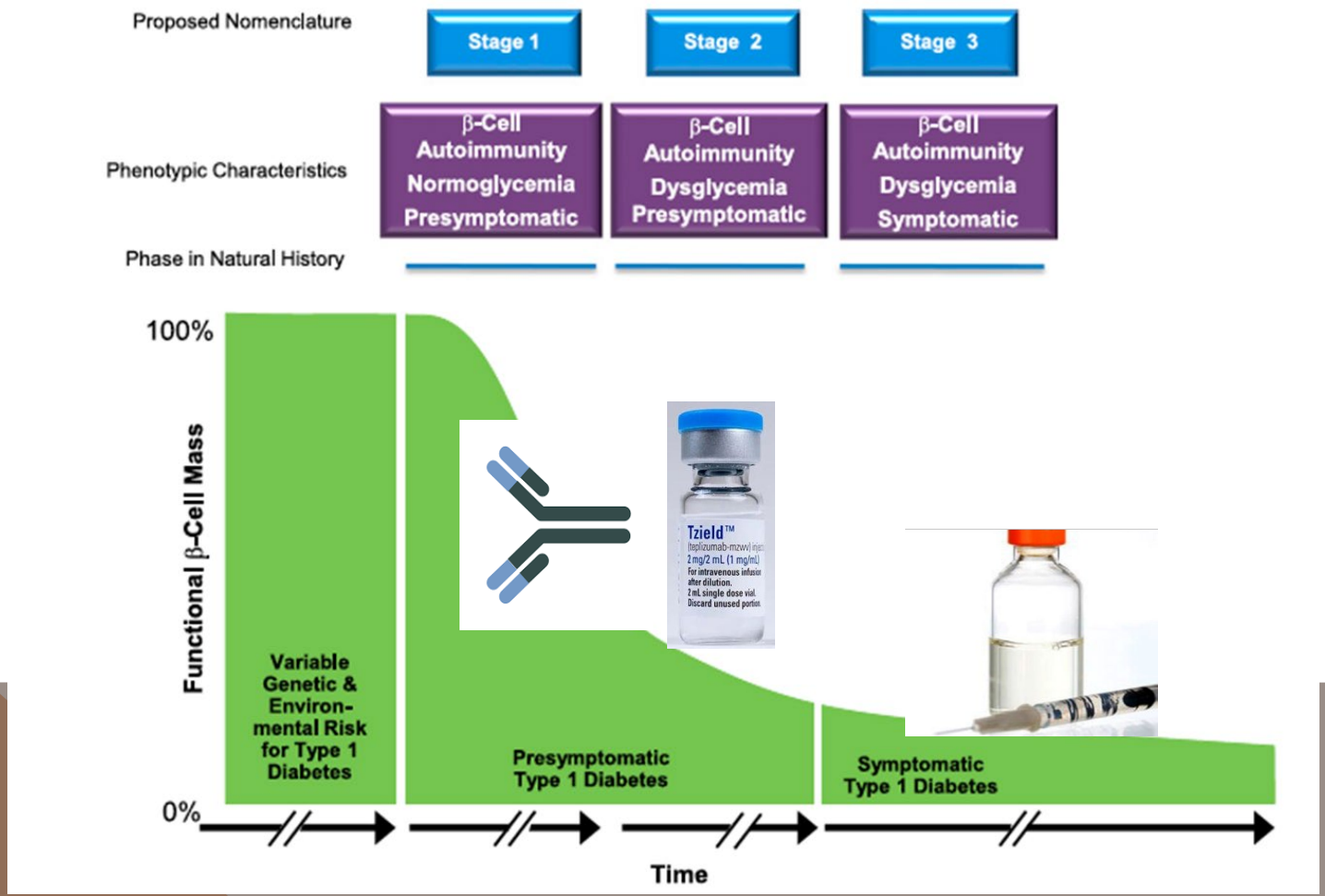
Common and increasing autoimmune disease

Heterogenous disease – children and adults

Predictable – genetic testing and measure islet autoantibodies

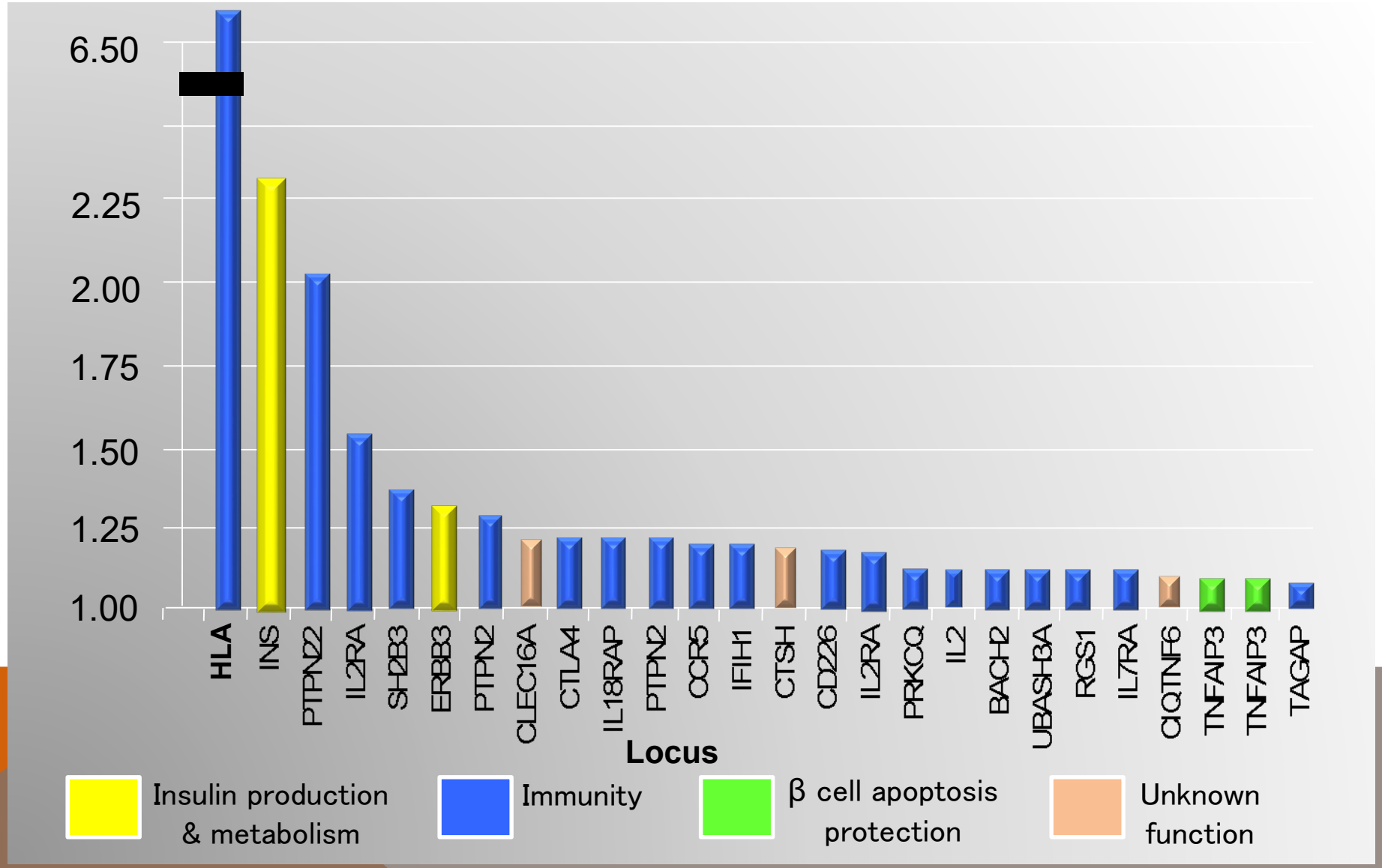
Immune intervention can impact the clinical development of type 1 diabetes

# STAGES OF TYPE 1 DIABETES DEVELOPMENT



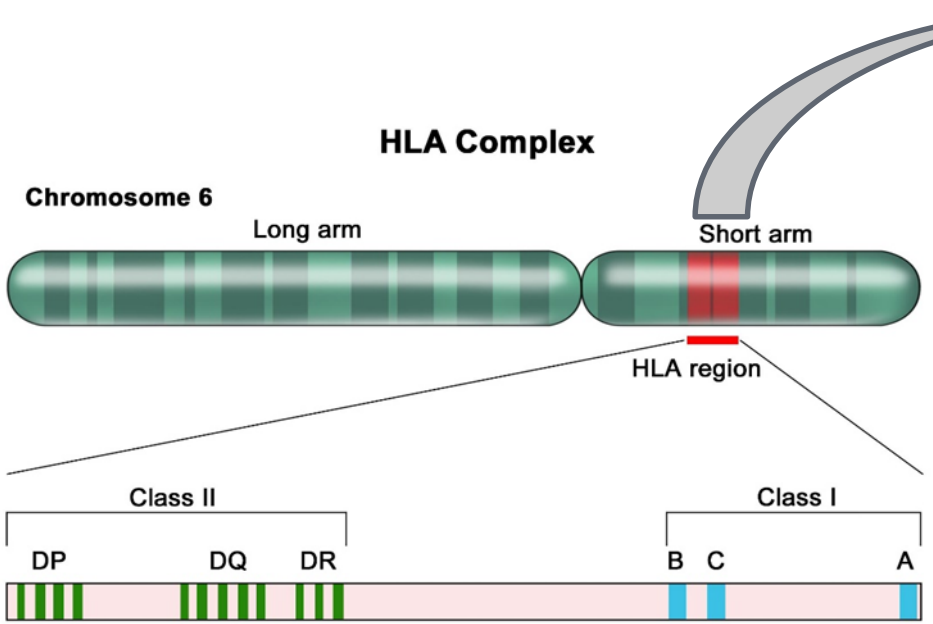

Insel RA, et al. Diabetes Care 2015.

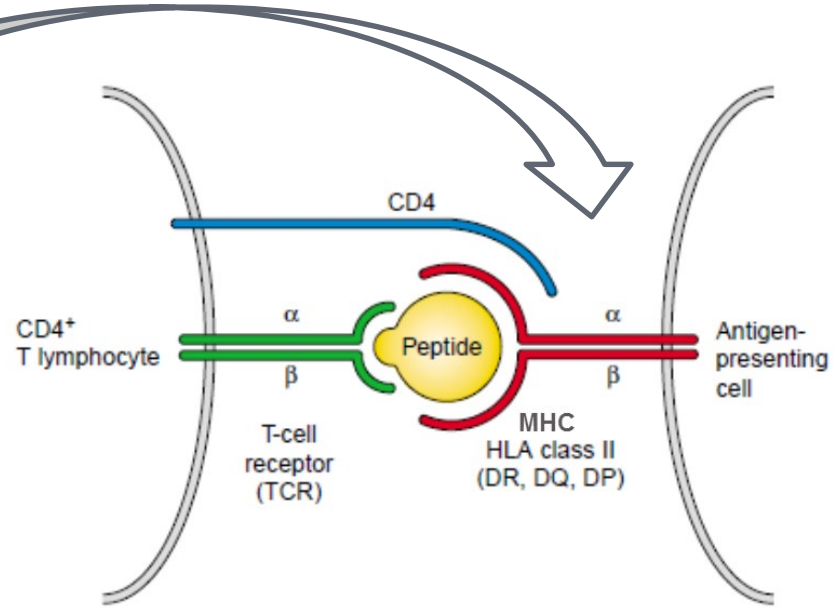
# GENETICS OF TYPE 1 DIABETES




Concannon et al. N Engl J Med. 2009.

# HLA GENES IMPART GENETIC RISK AND PROTECTION FOR TYPE 1 DIABETES

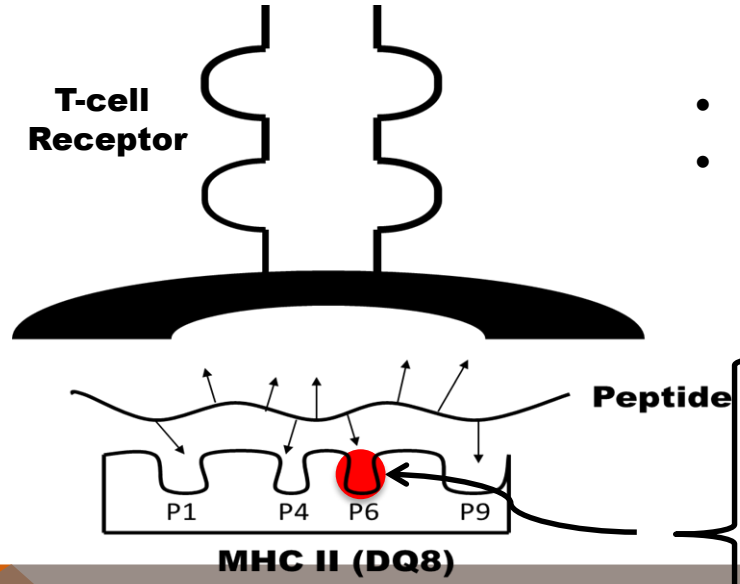


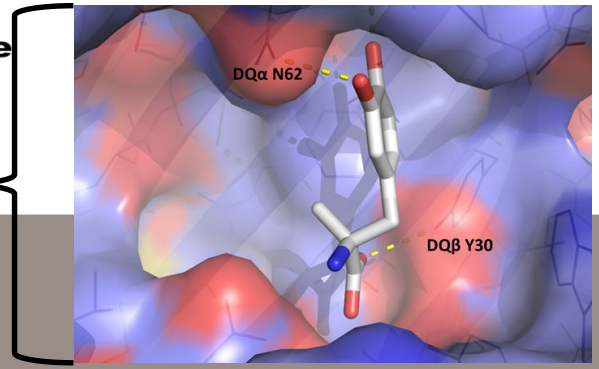

| HLA-DQ | Odds Ratio |
|---|---|
| **DQ8** (*DQA1*03:01, DQB1*03:02*) | **~11** |
| **DQ2** (*DQA1*05:01, DQB1*02:01*) | **~4** |
| **DQ6** (*DQA1*01:02, DQB1*06:02*) | **0.03** |

How insulin peptides are presented by HLA molecules is critical for T cell function.

# PERSONALIZED MEDICINE
# BLOCK HLA-DQ8 WITH METHYLDOPA

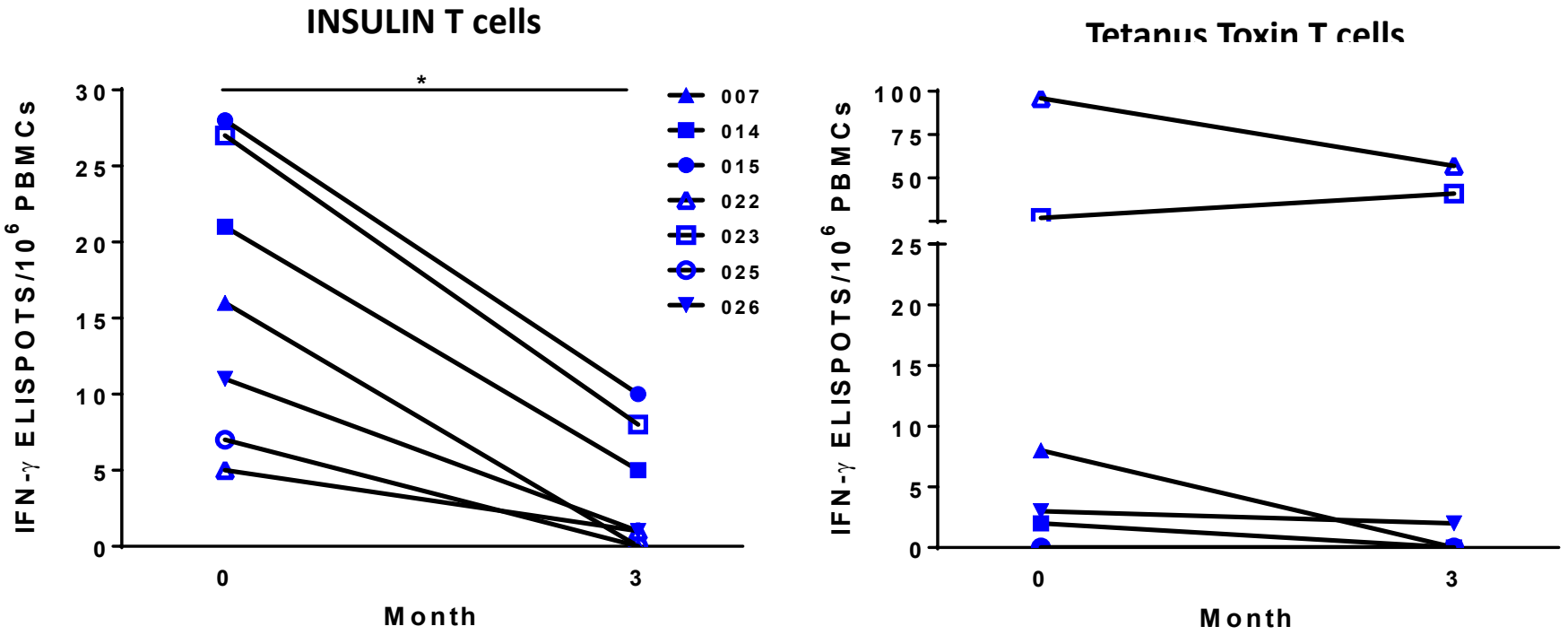



- Oral drug to treat hypertension in children and adults.
- Clinically well-established.
- Able to bind and specifically block DQ8 self-peptides to T cells.




Ostrov DA, et al. J Clin Invest 2018.

# METHYLDOPA BLOCKS DISEASE SPECIFIC T CELLS IN T1D



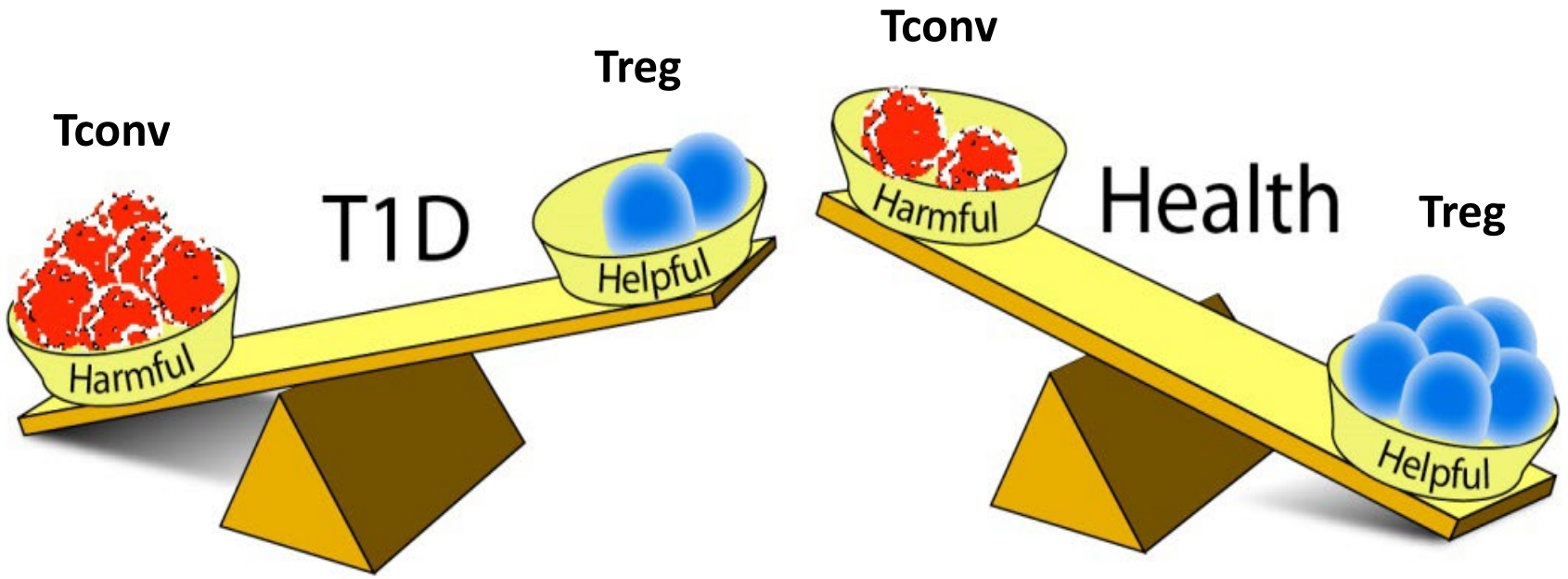


*Nakayama M, . . . Michels AW. PNAS 2015.

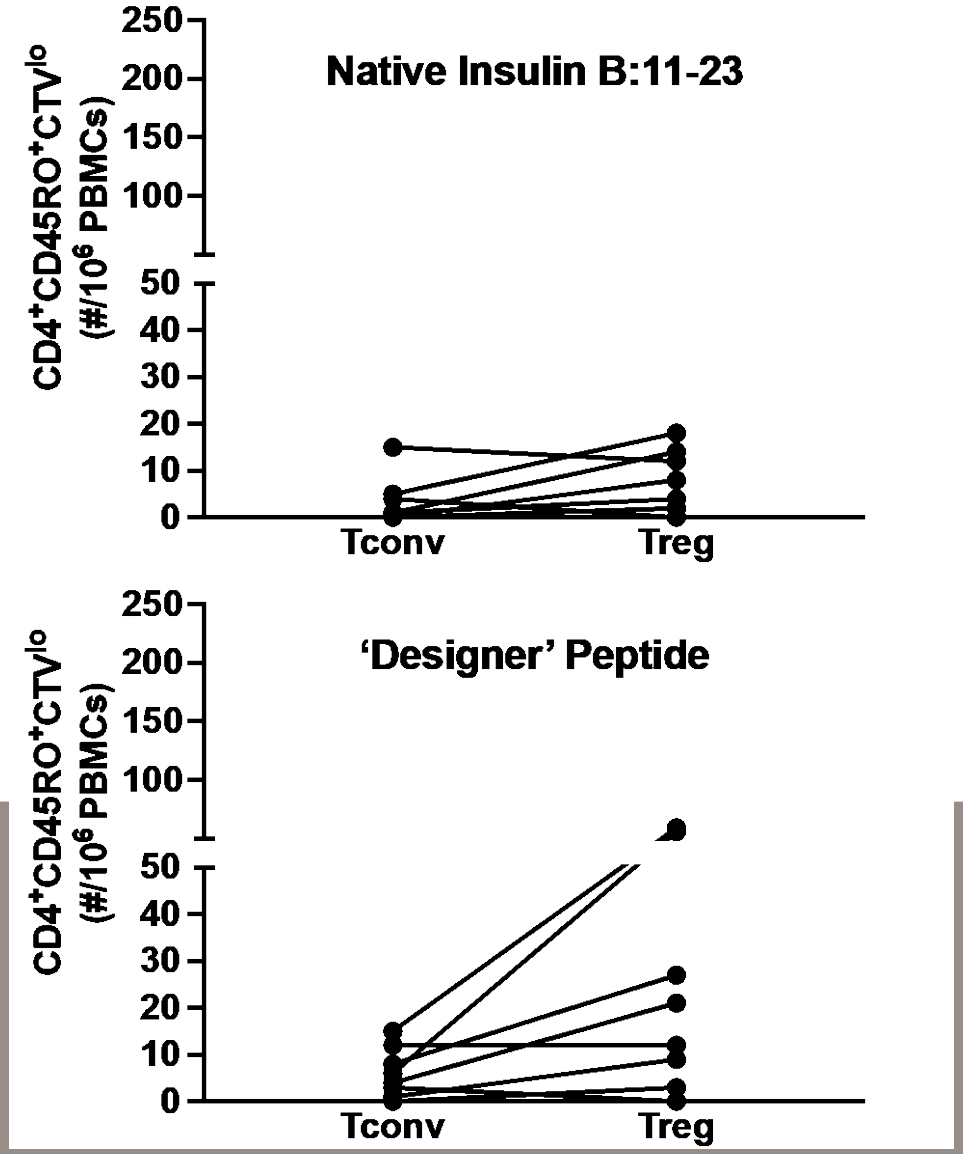
*Michels AW, . . . Nakayama M. Diabetes 2017.

*Spanier JA, . . . Fife BT. Diabetes 2017.

# PREVENT AND TREAT T1D BY SAFELY REEDUCATING THE IMMUNE SYSTEM



# INSULIN-BASED VACCINE

# SUMMARY

- Type 1 diabetes can be diagnosed before symptoms develop
- There is now a clinical treatment available to delay the onset of stage 3 (insulin requiring) type 1 diabetes
- The future for prevention and delay of type 1 diabetes is hopeful

# QUESTIONS?

#EPICconf2024

www.EPICconferences.org