Finding and Treating Autoimmune Diseases

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GOALS
• What is autoimmunity?
• How does autoimmunity lead to type 1 diabetes?
• How do we screen for islet autoimmunity?
• What can we do to stop islet autoimmunity?
TYPE 1 DIABETES: AUTOIMMUNE BETA CELL DESTRUCTION

TYPE 1 DIABETES: INCIDENCE RISING 3-5% PER YEAR

Children <15 years old

1.4 million patients in U.S.A.

- Finland
- Colorado
- Germany

Slide courtesy M. Rewers
**PATHWAY TO TYPE 1 DIABETES**

- **ENVIRONMENTAL TRIGGER**
- **BETA CELL LOSS BEGINS**
- **CLINICAL ONSET**

**Islet Autoantibodies**
- Progressive loss of insulin release
- Immunological abnormalities

**GLUCOSE INTOLERANCE**


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**MULTIPLE ISLET AUTOANTIBODIES AND RISK OF PROGRESSION TO DIABETES IN CHILDREN**

- Progress to T1D:
  - 44% in 5 y
  - 70% in 10 y
  - 85% in 15 y

**T1D Disease Progression**

**The Stages to Type 1 Diabetes**

- **STAGE 1**
- **STAGE 2**
- **STAGE 3**
- **STAGE 4**

**AUTOIMMUNITY SCREENING FOR KIDS**

303-724-1ASK | ASKhealth.org

Approved by the Colorado Multiple IRB #14-0553
ASK Population: children 2-17 y old
Denver Metro Area 7 counties

5,000 screened Jan '17-Jan '18
~18,000 approached for consent
50,000 to be screened

ASK Goals:
1. Understand prevalence of islet autoimmunity in the Denver metro area
2. Enroll children in prevention studies
3. Prevent DKA (Diabetic ketoacidosis) at diagnosis of diabetes
4. Reduce morbidity in children with undiagnosed celiac disease

PREVENTING TYPE 1 DIABETES

Simmons et al., 2016
IMMUNE TARGETS IN TYPE 1 DIABETES

Bluestone et al., 2010

WHAT HAS WORKED?

Adapted from Bluestone et al., 2010

Anti-CD3
Anti-CD20
Rituximab
CTLA-4 (Abatacept)
Alefacept

C-PEPTIDE TO ASSESS β-CELL FUNCTION

A SINGLE COURSE OF ANTI-CD3 IN NEW ONSET T1D IMPROVES INSULIN SECRETION FOR 2 YEARS

**p<0.02

PROTÉGÉ - 14-DAY TEPLIZUMAB PRESERVES C-PEPTIDE IN SUBGROUPS 2 YEARS AFTER TREATMENT

Phase 3

Hagopian et al., Diabetes, 2013

ABATACEPT DELAYS FALL IN C-PEPTIDE 3 YEARS AFTER INITIAL TREATMENT

Phase 2

Orban et al., Diabetes Care, 2014

RITUXIMAB DELAYS FALL IN C-PEPTIDE 2 YEARS AFTER INITIAL TREATMENT

Phase 2

Pescovitz et al., Diabetes Care, 2014

WHERE ARE WE GOING?

adapted from Bluestone et al., 2010

STAGE 1
AUTOANTIBODY POSITIVE normal glucose tolerance

STAGE 2
AUTOANTIBODY POSITIVE Dysglycemia

STAGE 3
NEW-ONSET T1D

TrialNet CTLA-4 (Abatacept)

TrialNet Methyldopa

TrialNet Hydroxychloroquine
SUMMARY
1. Type 1 diabetes is now defined by stages from autoimmunity to abnormal blood sugars.
2. Screening can help identify children before they have symptoms.

FOR MORE INFORMATION
www.childrensdiabetesfoundation.org
www.jdrf.org
www.trialnet.org
www.immunetolerance.org

Questions?