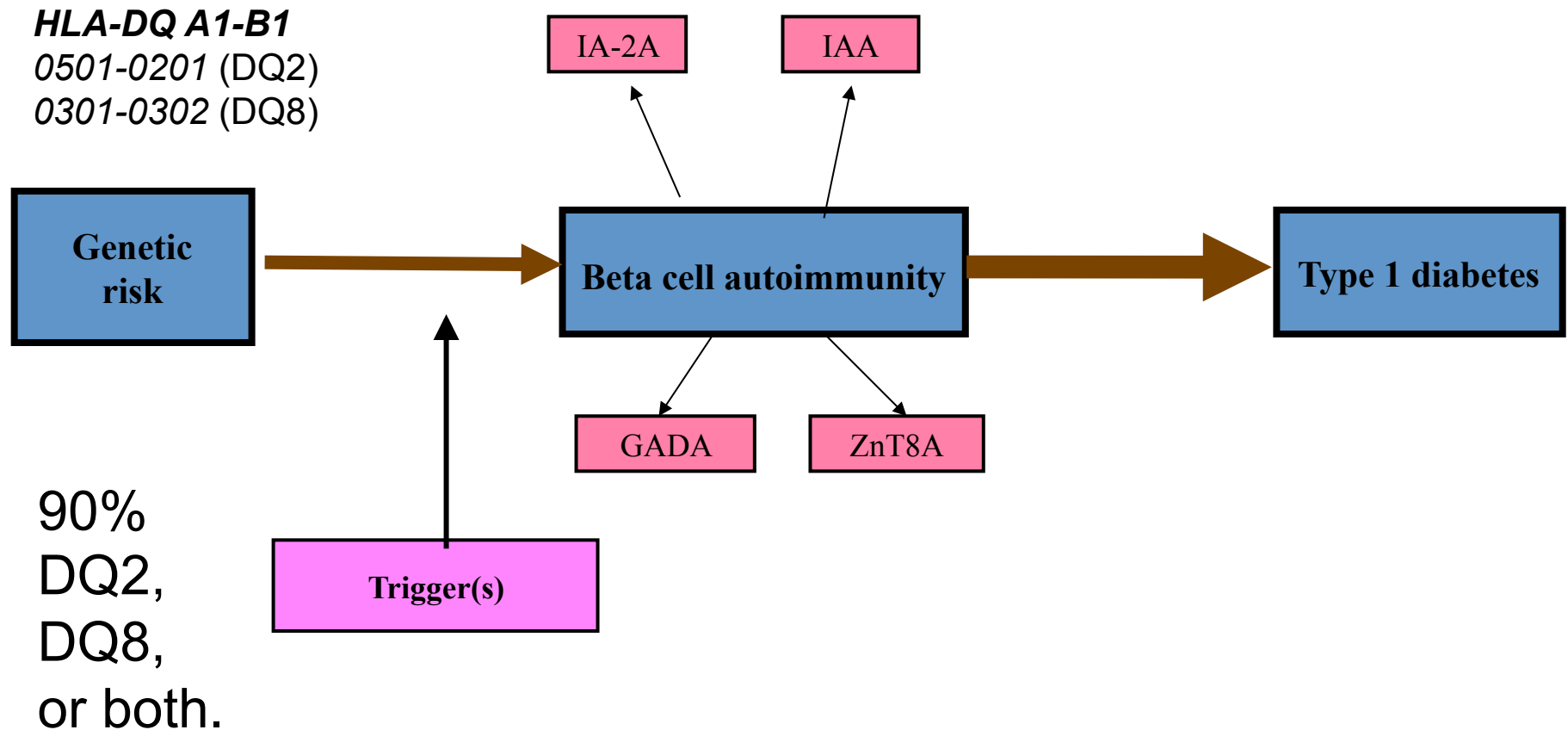


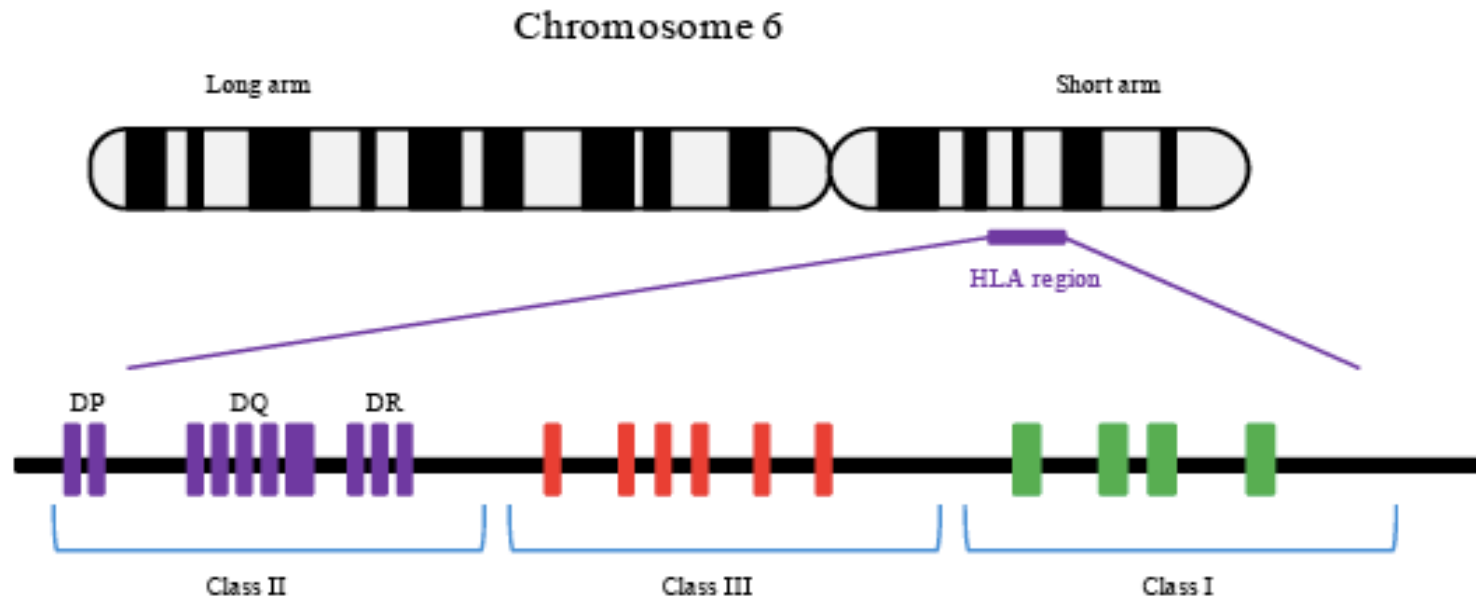
# DIABETESFORUM 2013

- Diabetes nu och i framtiden:
- **VAD HÄNDER FRAMÖVER?**
- **Är diabetes typ-1 en autoimmun sjukdom?**
- Kan TEDDY hjälpa till att besvara frågan?

Type 1 diabetes is a model disease for prediction and prevention of an autoimmune disease.

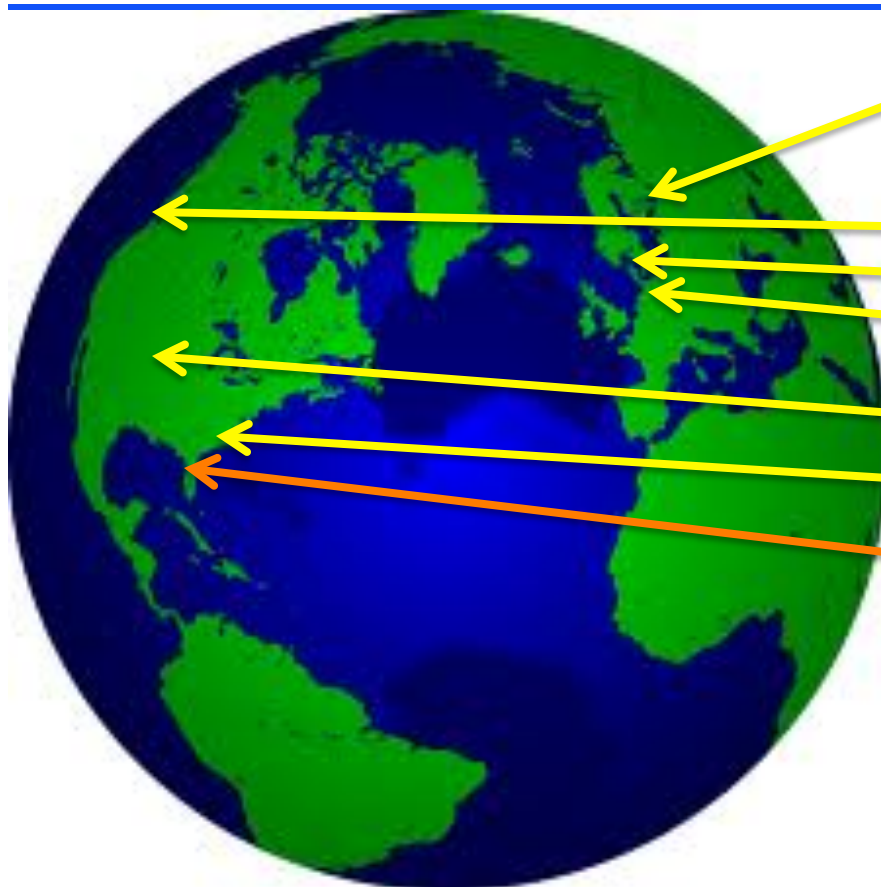


# HLA risk is the basis for primary prevention.



Rank order: DQ2/8; DQ8/8; DQ8/6.4; DQ8/5.1; DQ2/2; DQ8/4; DQ8/6.3 and DQ2/6.4.

These genotypes account for 70% of T1D patients and 16% of newborns.



FINLAND Olli Simell (jorma Toppari)

WASHINGTON William Hagopian

SWEDEN Åke Lernmark

GERMANY Anette Ziegler

COLORADO Marian Rewers

GEORGIA/FLORIDA Jin-Xiong She

DATA COORDINATING CENTER  
Jeffrey Krischer

NIH liason Beena Akolkar

More than 150 employed; 25 M\$/year

### TEDDY Committees:

Genetics

Immune markers

Infectious agents

Psychosocial

Celiac Disease

Clinical Implementation

Coordiantors

Bill Hagopian & Steve Rich

Ezio Bonifacio & Åke Lernmark

Heikki Hyöty & Eric Triplett

Suzanne Johnson & Barbro Lernmark

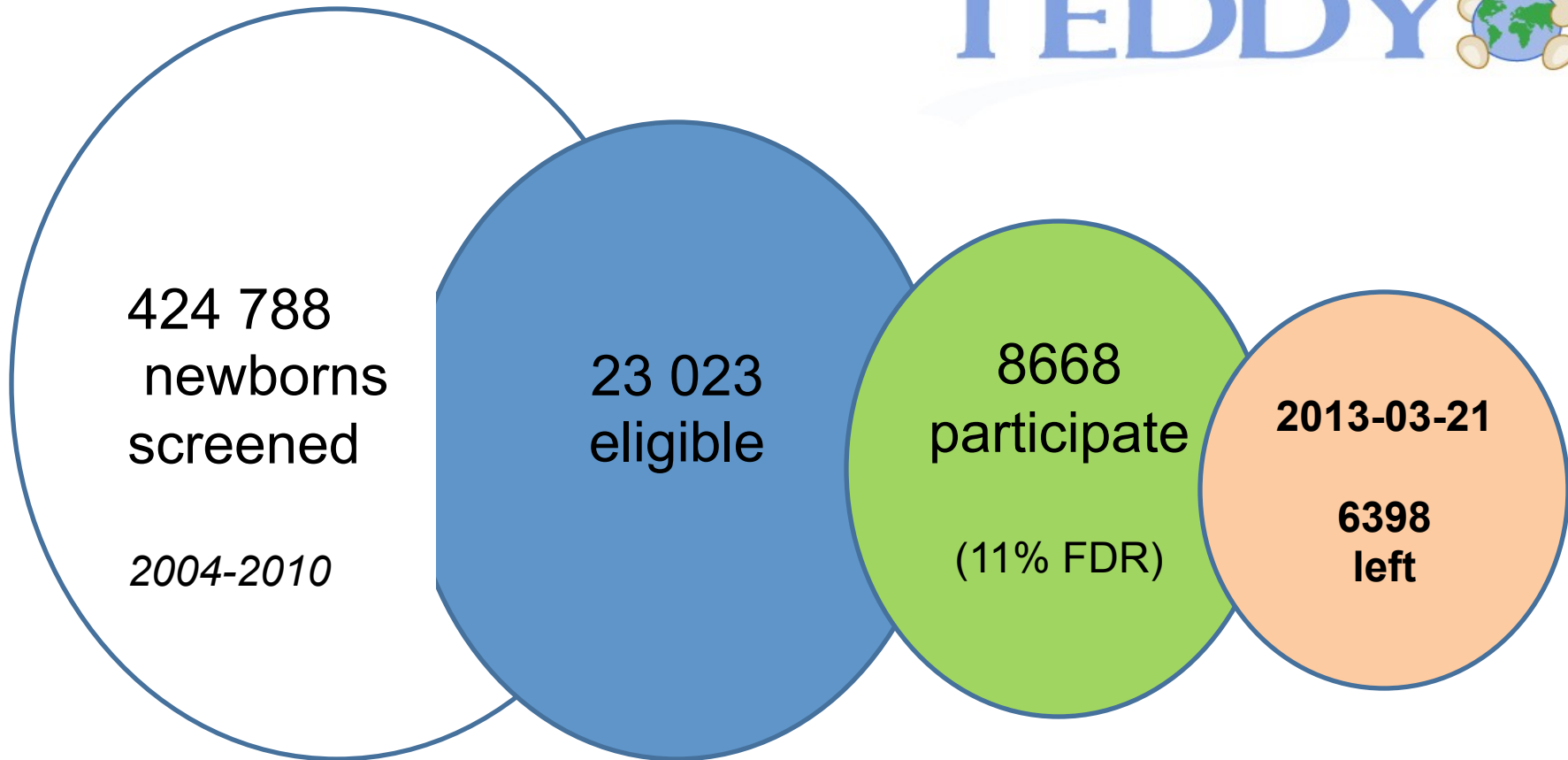
Daniel Agardh & Olli Simell

Helena Larsson & Mike Haller

Judy Baxter & Tuula Simell



# Screening newborns for type 1 diabetes risk.

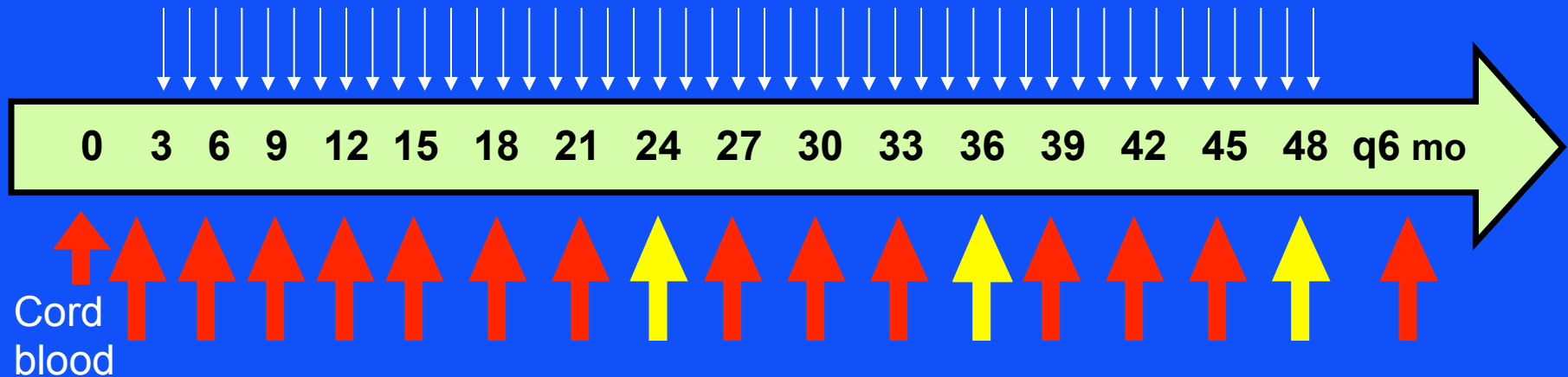


# DEFINITIONS

- ISLET AUTOIMMUNITY:
  - autoantibodies against
    - insulin, GAD65, IA-2 as well as ZnT8
    - persistent: more than two visits
    - confirmed: both reference laboratories agree
- TYPE 1 DIABETES
  - diagnostic criteria recommended by the American Diabetes Association (ADA)
    - OGTT 2 hr value is a common diagnosis in TEDDY

# TEDDY Follow-up visits

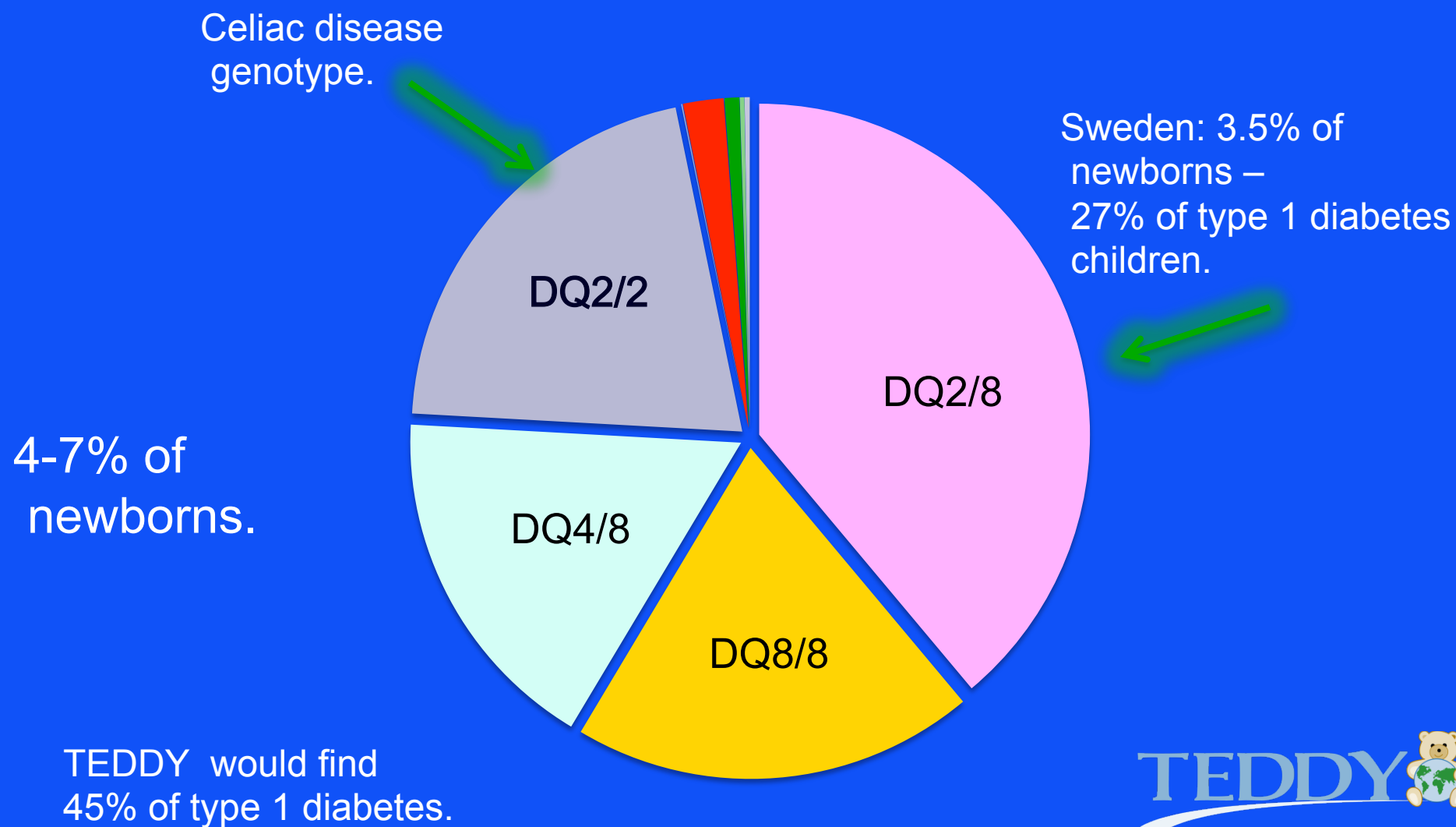
Stool samples collected monthly



Clinic visits every 3 months (blood samples, physical exam diet records, etc.)

↑ From 24 months: tTG autoantibodies (TGA) are measured annually.

# HLA-DQ genotypes in TEDDY.





# WHAT ARE WE TRYING TO DO?

---

- Identify triggers of islet autoantibodies.
  - What have the children been exposed to that made them develop islet autoantibodies?
- Once autoantibodies have developed what factors determines if the child will go on to develop diabetes?

# TEDDY numbers.

March 16, 2013

Islet autoantibodies:

Persistent (more than one visit)

Confirmed (two labs agree)

**Ab+: 473/7800 (6%)**

**GP: 367      FDR: 106**



# RISK FACTORS FOR AUTOANTIBODIES.

## Before birth

- Greater birth weight and length.
- "Older" mother.
- Infections during pregnancy.

## After birth

- Infections reported two visits before the autoantibodies.
  - Upper respiratory infections with fever.

# TEDDY Numbers.

March 16, 2013

Type 1 diabetes.

Often diagnosed at a TEDDY visit by  
OGTT.

T1D: 148

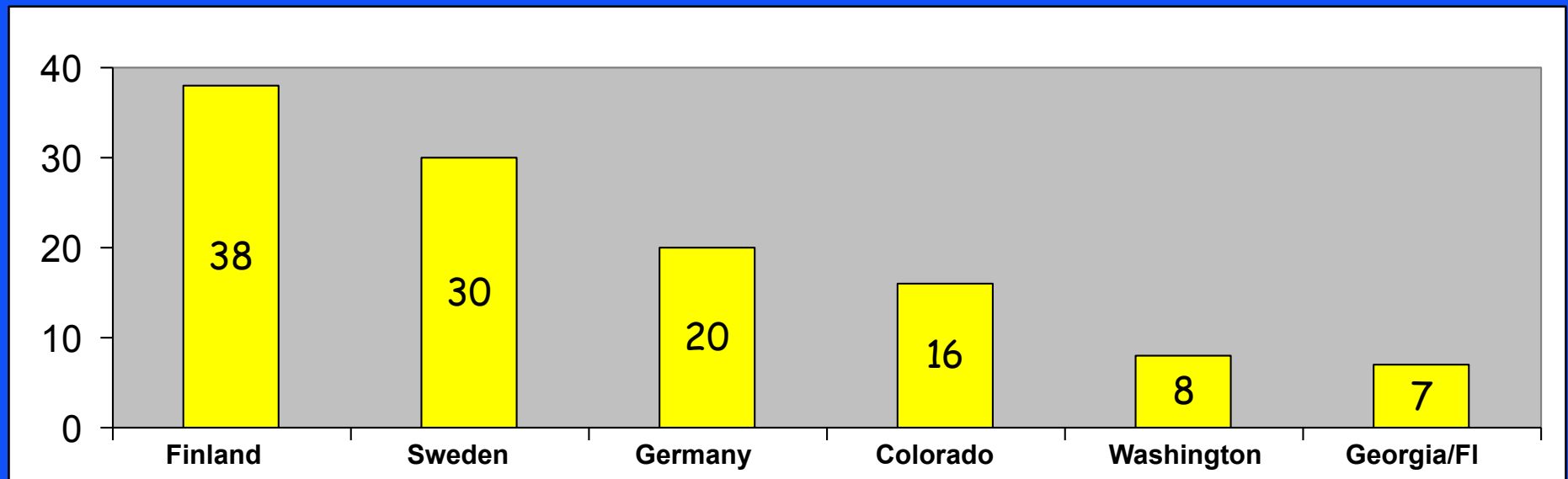
GP: 96

FDR: 52



# Type 1 diabetes by country.

- N=119
  - 54 F/65 M
- Autoantibodies in T1D children:
  - 4 negative (3 %)
  - 115 positive Ab (97 %)



Data current as of August 31, 2012

# SECOND PRIMARY ENDPOINT

Children with islet autoantibodies do indeed progress to type 1 diabetes:

**Reduced Prevalence of Diabetes Ketoacidosis at Diagnosis of Type 1 Diabetes in Young Children Participating in Longitudinal Follow-Up**

*Diabetes Care* 34:1–6, 2011

Elding Larsson H, Vehik K, Bell R, Dabelea D, Dolan L, Pihoker C, Knip M, Veijola R, Lindblad B, Samuelsson U, Holl R, Haller MJ; TEDDY Study Group; SEARCH Study Group; Swediabkids Study Group; DPV Study Group; Finnish Diabetes Registry Study Group.



# ✓ VAD HÄNDER FRAMÖVER?

Prediktion förbättras:

screena skolbarn?

Symptomfri diagnos

# ✓ Är diabetes typ-1 en autoimmun sjukdom?

Ja – verkar inte bättre – dags för:

**autoimmun diabetes?**

# ✓ Kan TEDDY besvara frågan?

# Vad händer framöver i TEDDY?

418 Children with 1 or more persistent confirmed antibodies.

114 Children who went on to develop T1D.

1:3 Matching cases:controls

- Dietary biomarkers
  - Fatty acids
  - Vitamin D
  - Ascorbic acid
- Metabolomics
  - Plasma

1:1 Matching cases:controls

- Gene Expression
  - mRNA
- Microbiome
  - Stool
- Viral metagenomics
  - Plasma



# TEDDY



# THANK YOU!

The Environmental Determinants of Diabetes in the Young