Is the Gut Microbiome Associated with Residual *-Cell Function and Development of Complications in Individuals with Longstanding Type 1 Diabetes Mellitus

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Objective: 1. To investigate whether T1D individuals with preserved β-cell function exhibit a distinct gut microbial and circulating immune cell signature, leading to a reduced incidence of diabetes complications (CVD, nephropathy,...

Ethical review	Approved WMO
Status	Pending
Health condition type	Diabetic complications
Study type	Observational non invasive

Summary

ID

NL-OMON56647

Source
ToetsingOnline

Brief title
MARVEL cohort

Condition

- Diabetic complications
- Autoimmune disorders

Synonym
Type 1 diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: NWO

Intervention

Keyword: Betacell function, Complications, Microbiome, Type 1 Diabetes

Outcome measures

Primary outcome

Main study parameters/endpoints: The primary endpoint is long-term residual β-cell function as assessed by baseline and stimulated 2-hour post meal urinary C-peptide levels at 3,6 and 10 years follow-up.

Secondary outcome

The secondary endpoint pertains presence and incidence of diabetes complications (cardiovascular disease, nephropathy, neuropathy and retinopathy), gut microbiota composition measured in feces with shotgun sequencing, glucose time-in-range (CGM-metrics) and subsequent exogenous insulin dose. Tertiary endpoints include the profiling of immune cell subsets, assessment of autoreactive T lymphocytes and HLA typing by high resolution sequencing of circulating leukocytes (IMMOCHIP) in relation to untargeted plasma metabolomics (Metabolon).

Study description

Background summary

Rationale: It has become apparent that most individuals with type 1 diabetes mellitus (T1D) have some remaining β-cell function. Individuals with T1D and a preserved β-cell function have a lower risk of hypoglycemia and diabetic

complications. The factors regulating residual β-cell function are unknown. A likely mechanism leading to β-cell preservation is regulation of immunological tone by the gut microbiome. Recently we published in a small pilot cohort (GUTDM1, METC 2020_105) that residual β-cell function is linked to better glycemic control (time in range) and linked to specific gut microbiota composition. Since this cohort was too small to also show a link with presence of diabetes complications and recruit enough individuals with preserved β-cell function for confirmatory intervention trials to increase β-cell function, we will now aim to recruit a larger follow-up cohort to a) investigate whether residual β-cell function is associated with gut microbiome composition and circulating immune cell counts in individuals with T1D from the new Diabeter Center Amsterdam and b) identify 500 potential eligible individuals with preserved β-cell function.

Study objective

Objective: 1. To investigate whether T1D individuals with preserved β-cell function exhibit a distinct gut microbial and circulating immune cell signature, leading to a reduced incidence of diabetes complications (CVD, nephropathy, neuropathy, and retinopathy).
2. Identify individuals with preserved β-cell function for diagnostics as well as future intervention studies to increase β-cell function.
Study design: 10-year longitudinal observational cohort study

Study design

a 10 year multicenter logitudinal cohort study

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: This study is considered a low-risk study. The patient will complete several questionnaires, keep track of a food diary and collect urine and feces prior to the study visit. At the study visit we will require a fasted plasma sample, this will slightly increase the chances of a hypoglycemic episode, largely mitigated because all participants carry a continues glucose monitor. Additionally, we will calculate BMI, waist circumference, liver stiffness and measure blood pressure. The questionnaires inquire about the burden of diabetic complications, socio-economic status and financial literacy, abdominal complaints and hypoglycemic episodes and comorbidities associated with diabetes. We argue that the risk and discomfort associated with this study is similar to the yearly diabetes check-up and justified in light of the potentially profound insights and novel treatments to be gained by studying the impact of the gut microbiome on residual β-cell function in T1D.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Everyone with type 1 diabetes above the age of 18

Exclusion criteria

1. Active infection during the study visit
2. Inability or unwillingness to donate feces or urine.
3. Smoking or illicit drug use (e.g. MDMA/amphetamine/cocaine/heroin/GHB) in the past three months or use during the study period.
4. Inability or unwillingness to provide informed consent.
5. Absence of a large bowel (ie colostomy)

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2023
Enrollment:	5000
Type:	Anticipated

Ethics review

Approved WMO

Date:	28-02-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	12-08-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL85375.018.23