Onderzoek naar de oorzaak van familiaire hypercholesterolemie bij patiënten zonder een bekende genetische oorzaak

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON27045

Source
NTR

Brief title
BEAVER

Health condition

Familial hypercholesterolemia
Genetics
Cholesterol
LDL

Familiaire hypercholesterolemie
Genetica

Sponsors and support

Primary sponsor: Academisch Medisch Centrum, Amsterdam
Source(s) of monetary or material Support: ZonMW

Intervention

Outcome measures

Primary outcome

- SNP’s and DNA methylation percentage will be analysed using a multivariable linear regression analyses.

- RNA sequencing and gene expression will be expressed relative to controls, and in a subgroup with and without LLT.

- Protein and lipid content measured through mass spectrometry will be expressed as relative abundance in subjects (on and off LLT) and controls. Heatmaps will be used to display relative differences between groups.

- Protein assessed with ELISA assays will be expressed as means and compared with a student’s t-test.

- Fast protein liquid chromatography (FPLC) on lipoprotein cholesterol levels will be expressed as means and compared with a student’s t-test.

Secondary outcome

none

Study description

Background summary

Familial hypercholesterolemia (FH) is characterized by increased low density lipoprotein (LDL) cholesterol and increased cardiovascular risk. There are 3 known genes (LDLR, ApoB, PCSK9) in which mutations can lead to the FH phenotype (FH1 to 3 respectively). However, in approximately 5-10% of patients such a mutation cannot be found, despite family-based linkage studies (the so called FH4 group). Therefore, a more elaborate approach is deemed necessary. In this study we will combine data derived from the genome, epigenome, transcriptome, proteome, and metabolome to find novel genes and metabolic pathways in lipid metabolism.

Study objective

Familial hypercholesterolemia (FH) is characterized by increased low density lipoprotein (LDL) cholesterol and increased cardiovascular risk. There are 3 known genes (LDLR, ApoB, PCSK9) in which mutations can lead to the FH phenotype (FH1 to 3 respectively). However, in approximately 5-10% of patients such a mutation cannot be found, despite family-based

linkage studies (the so called FH4 group). Therefore, a more elaborate approach is deemed necessary, where data derived from the genome, epigenome, transcriptome, proteome, and metabolome are combined to find novel genes and metabolic pathways in lipid metabolism.

Study design

Visit 1: under lipid lowering therapy

Visit 2: after discontinuation of lipid lowering therapy for 4 weeks

Intervention

none

Contacts

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Eligibility criteria

Inclusion criteria

- Diagnosis of familial hypercholesterolemia based on Dutch Lipid Clinic Network criteria (Nordestgaard et al. 2013) in combination with a negative DNA-testing (mutations in LDLR, ApoB, PCSK9).

- Untreated LDL-cholesterol levels of > 95th percentile for age and gender

- >18 years of age

Exclusion criteria

 Abusive alcohol use

 Dysthyroidism

 Pregnancy, breastfeeding

 Diabetes mellitus

 Use of medication that might elevate lipid levels

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-01-2018
Enrollment:	100
Type:	Anticipated

Ethics review

Positive opinion

Date:	27-02-2018
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 44591
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL6881
NTR-old	NTR7059
CCMO	NL62407.018.17
OMON	NL-OMON44591

Study results