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

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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...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON27045

Bron
Nationaal Trial Register

Verkorte titel
BEAVER

Aandoening

Familial hypercholesterolemia
Genetics
Cholesterol
LDL

Familiaire hypercholesterolemie
Genetica

Ondersteuning

Primaire sponsor: Academisch Medisch Centrum, Amsterdam
Overige ondersteuning: ZonMW

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- 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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

Visit 1: under lipid lowering therapy

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

Onderzoeksproduct en/of interventie

none

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- 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

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

 Abusive alcohol use

 Dysthyroidism

 Pregnancy, breastfeeding

 Diabetes mellitus

 Use of medication that might elevate lipid levels

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	17-01-2018
Aantal proefpersonen:	100
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	27-02-2018
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 44591
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten