B cell monitoring in healthy donors, smokers and CAD patients

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

Samenvatting

ID

NL-OMON26137

Bron
Nationaal Trial Register

Verkorte titel
CHDR1836

Aandoening

cardiac arrest

Ondersteuning

Primaire sponsor: CHDR
Overige ondersteuning: CHDR

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Primary study parameters/outcome of the study:
Circulating B cell subsets:

- B1 cells
- Naive B cells
- Transitional B cells
- Non-class-switched memory B cells
- Class-switched memory B cells
- Plasmablasts and plasma cells
- Regulatory B-cells
- Age associated B-cells

lmmunoglobulin classes:
- total lgG, lgM, lgE. oxLDL lgG1, lgG2 + lgM.
- oxLDL specific lgM and lgG ELlSpot

B cell functionality, by means of ex vivo challenges, evaluating:
- Pathways:
. TLR7 stimulation
. TLR9 stimulation
- Readouts:
[] Circulating cytokines (e.g. lL-10 and lL-35 + lL-12p70,lL-1β, TNFa, lL-6, lL-17)
[] Secreted cytokines after stimulation (e.g. lL-10, lL-35, TGFβ, pro-inflammatory cytokines)
[] lntracellular cytokines (e.g. lL-10, lL-35)
[] Surface markers on B-cells (non-lineage markers) (e.g. PD-1, PDL-1 , PDL-2, TIM-1)
- Other relevant immune cells including, but not limited to:
o CD4+ T cells (Th1/Th2/Th17/Treg), CD8+ T cells, inflammatory monocytes, neutrophils, basophils
- Routine laboratory blood tests:
o Chemistry
o Hematology
- lmmune cells in adipose tissue

Toelichting onderzoek

Achtergrond van het onderzoek

The study will be conducted to determine if there are differences in circulating B cell subsets between healthy volunteers and patients with stable coronary artery disease. Next to this also the effect of aging will be assessed by measuring young healthy volunteers (18 - 25 years) versus elderly (>60 years) healthy volunteers. To correct for medication use by patients with stable coronary artery disease, 2 groups of healthy volunteers that smoke will be included. If a difference is found between groups then this may be a target for future drug development.

Doel van het onderzoek

Atherosclerosis is a chronic inflammatory disease of the artery wall. Treatment of atherosclerosis has been based on lipid lowering therapies for years, reducing multiple risk factors. Adaptive immunity plays a key role in the pathogenesis of atherosclerosis. Accumulating evidence supports the idea that immunization with antigenic proteins or peptides may reduce atherosclerosis. Modulation of the adaptive immune system may treat or prevent atherosclerosis, and lead to the development of more selective and less harmful interventions, while keeping host defense mechanisms against infections and tumors intact. Aging is one of the major drivers of atherosclerosis and with a rapidly increasing aging population, there is a huge need to enhance our understanding of immune responses during cardiovascular disease to develop the most effective therapeutic intervention for the patient. Although the role of T cells in the development and progression of atherosclerosis has been extensively studied for decades, only recently the role of B cells has gained more attention. B cell subsets are found in human and murine atherosclerotic plaques. B cells have long been thought to have a general protective effect in atherosclerosis. However, recent studies have identified differential effects of different B-cell subsets. B1 cells are atheroprotective, mainly via the production of natural IgM antibodies that bind oxidized low-density lipoprotein and apoptotic cells. B2 cells are suggested to be proatherogenic, via production of IgG, secretion of TNFα, and activation of CD4 T cells. Finally, there is a minor subset of splenic regulatory B cells (Bregs) that protect against atherosclerotic inflammation by promoting the generation of Tregs and production of anti-inflammatory cytokines IL-10 and TGF-β and proapoptotic molecules. It is unknown whether Bregs are a permanently existing cell subset, or derived from B cells upon specific stimulation.

Onderzoeksopzet

The total duration of the study for each subject will be 1-2 hours.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Healthy volunteers:
1. healthy male subjects (18-25 years or >60 years);
2. ability to participate, and willingness to give written informed consent and to comply with the study restrictions.
3. BMI 18 - 28
4. non-smoking, elderly non-smoking for at least 15 years.

Smokers:
1. male subjects (18-25 years or >45 years)
2. ability to participate, and willingness to give written informed consent and to comply with the study restrictions.
3. BMI 18 - 28
4. volunteers >45 years: smoking for at least 15 packyears, volunteers 18- 25 years: at least ½ pack a day for 6 months.

CAD patients:
1. male patients (>60 years) with proven stable atherosclerotic coronary artery disease defined as having undergone a revascularization procedure followed by a period of at least one year without signs or symptoms of coronary artery disease;
2. having one of the following risk factors: high cholesterol, smoking, diabetes, hypertension, or familiar risk.
3. ability to participate, and willingness to give written informed consent and to comply with the study restrictions.
4. BMI 18 - 28

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Healthy volunteers:
1. evidence of any active or chronic disease or condition (based on medical history, a physical examination, and vital signs) that could, in the opinion of the investigator, interfere with the study objectives;
2. evidence of any active or chronic disease or condition that affects the immune system.
3. having one of the following risk factors for CAD: high cholesterol, smoking, diabetes, hypertension, or familiar risk.
4. the use of any medication or vitamin/mineral/herbal/dietary supplement within less than 5 half-lives prior to study participation is prohibited, if the Investigator judges that it may interfere with the study objectives. The use of paracetamol (up to 4 g/day) is allowed;

5. body weight < 50 kg; BMI <18 or >28.
6. subject is pregnant or breast feeding;
7. smoking or current substance abuse, including alcohol and drugs;
8. loss or donation of blood over 500 mL within three months prior to participation;
9. unwillingness or inability to comply with the study protocol for any other reason.

Smokers:
1. evidence of any active or chronic disease or condition (based on medical history, a physical examination, and vital signs) that could, in the opinion of the investigator, interfere with the study objectives;
2. body weight < 50 kg; or BMI <18 or >35;
3. substance abuse, including alcohol and drugs;
4. loss or donation of blood over 500 mL within three months prior to participation;
5. unwillingness or inability to comply with the study protocol for any other reason.
CAD patients:
1. evidence of any active or chronic disease or condition other than stable CAD (based on medical history, a physical examination, and vital signs) that could, in the opinion of the investigator, interfere with the study objectives;
2. evidence of any active or chronic disease or condition other than stable CAD that affects the immune system.
3. body weight < 50 kg; BMI <18 or >28.
4. substance abuse, including alcohol and drugs;
5. loss or donation of blood over 500 mL within three months (males) prior to participation;
6. unwillingness or inability to comply with the study protocol for any other reason.

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:	01-02-2019
Aantal proefpersonen:	150

Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Positief advies

Datum:	21-05-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7754
Ander register	Stichting BEBO : N168390.056.19

Resultaten