# Translating biomarkers from animal models to the clinic: validating assays in healthy volunteers.

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The aim of our study is to identify the same 4 circulating analytes identified in the animal models in human subjects. An additional task will be to measure the basal levels and the inter-individual variability.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational invasive

# Summary

#### ID

NL-OMON35748

**Source** ToetsingOnline

**Brief title** IBATH (Identified biomarkers in animals translated to human)

## Condition

- Heart failures
- Cardiac and vascular disorders congenital

**Synonym** "cardiac hypertrophy", "heart failure"

**Research involving** Human

## **Sponsors and support**

Primary sponsor: Universiteit Maastricht Source(s) of monetary or material Support: CTMM

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## Intervention

Keyword: inflammation, Translating, validation

#### **Outcome measures**

#### **Primary outcome**

Biomarkers of inflammation as measured in the peripheral blood.

#### Secondary outcome

Not applicable.

# **Study description**

#### **Background summary**

Heart failure (HF) is a leading cause of hospitalization and mortality. It is a common health problem particularly in the elderly. Existing biomarkers can only be used to monitor progression of HF and they cannot predict the disease before clinical symptoms become apparent.

Research over the last decades has provided strong evidence of inflammatory activity as an important pathway in early phase of HF. Seminal clinical data found raised plasma levels of cytokines in HF patients and subsequent animal experiments suggested that certain anti-inflammatory therapies may be beneficial.

The specific role of cytokines and chemokines is not yet dissected, but it is generally acknowledged that they play an important role in the cardiac remodeling and disease progression, particularly during early phases. Therefore our research group has investigated in animal models that develop left ventricle (LV) remodeling in response to pressure overload (TAC: transverse aortic constriction) or permanent myocardial infarction (MI) to identify the inflammatory mediators involved. The results indicate that in TAC mice a strong increase in circulating levels of at least 4 biomarkers take place. Interestingly, two out of these four molecules have never been described in literature as heart failure related. We identified that the same 4 biomarkers are elevated in serum of MI rats. The cardiac origin of these analytes was confirmed by analyzing homogenates of remote cardiac tissue, obtained from the septum. As a positive control, we demonstrate the presence of TIMP-1, a circulating inhibitor of matrix metalloproteinases, in both serum and tissue obtained from the infarct area of rat hearts.

The new potential biomarkers are offering advantages over the existing biomarkers used in the clinic: BNP and NT-proBNP. Indeed, the natriuretic

peptides are detectable only when the disease has been already established. Thus, the new putative biomarkers may be helpful in the early diagnosis and prognosis of HF.

#### **Study objective**

The aim of our study is to identify the same 4 circulating analytes identified in the animal models in human subjects. An additional task will be to measure the basal levels and the inter-individual variability.

#### Study design

15 males and 15 females according to the inclusion/exclusion criteria will be selected.

Each human subject will undergo a short questionnaire of 10 minutes to exclude significant disease and will give blood via venipuncture 2 times a day (one in the morning and one in the afternoon). At each session 15ml of blood will be withdrawn.

#### Study burden and risks

Inconvenience of blood sampling and spending time in our outpatient department.

# Contacts

**Public** Universiteit Maastricht

Universiteitssingel 50 6229ER NL **Scientific** Universiteit Maastricht

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# **Trial sites**

## **Listed location countries**

Netherlands

# **Eligibility criteria**

#### Age

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

#### **Inclusion criteria**

30 healthy people (15 males and 15 females) above 50 years of age. Such volunteers will be selected under the supervision of a physician-cardiologist who overall judges whether the person fulfills the general criteria for a healthy person.

## **Exclusion criteria**

Exclusion criteria will be a (chronic) inflammatory condition and use of anti-inflammatory drugs.

In a later stage, the levels of CRP, BNP and complement system proteins will be measured to confirm the absence of an inflammatory status. In case of high values, the subject will be informed and the blood sample will be dropped out from the study.

## Study design

## Design

Study type: Observational invasive		
Masking:	Open (masking not used)	
Control:	Uncontrolled	
Primary purpose:	Diagnostic	

#### Recruitment

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NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	20-01-2012

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Enrollment:	30
Туре:	Actual

# **Ethics review**

Approved WMO	
Date:	05-12-2011
Application type:	First submission
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

# **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 CCMO ID NL36328.068.11

# **Study results**

Date completed:	26-06-2012
Actual enrolment:	30