

# Understanding variability of immune responses to BCG vaccination: a systems biology approach

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To elucidate the host and environmental factors that influence the magnitude of the individual trained immunity responses to BCG vaccination using a systems biology approach.

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Immunodeficiency syndromes
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON45603

### Source

ToetsingOnline

### Brief title

Determinants of the response to BCG vaccine

### Condition

- Immunodeficiency syndromes
- Hepatobiliary neoplasms malignant and unspecified

### Synonym

BCG vaccine, tuberculosis vaccine

### Research involving

Human

### Sponsors and support

**Primary sponsor:** Radboud Universitair Medisch Centrum

**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** BCG vaccine, Innate immunity, Systems biology, Trained immunity

## Outcome measures

### Primary outcome

1) Immune cell function:

- ex vivo cytokine responses of monocytes
- immunophenotype of cell subpopulations

2) Genetic variation

3) Epigenetic, transcription and metabolic profiles relating to immune function of peripheral monocytes

4) Microbiome variation

### Secondary outcome

- Metadata (clinical, environmental data)
- Skin inflammation at vaccination site

## Study description

### Background summary

The Bacillus Calmette-Guérin (BCG) vaccine not only protects against infection with *Mycobacterium tuberculosis* and *Mycobacterium leprae*, but has also been shown to induce protection against a large number of unrelated pathogens. The non-specific effects of BCG lead to significant reduced infant morbidity and mortality. These striking effects are most likely mediated by the enhanced release of monocyte-derived cytokines resulting from epigenetic reprogramming of innate immune cells by BCG, a process that has been called trained immunity. However, the factors that influence the individual response to BCG vaccination remain largely unknown. A better understanding of the mechanisms involved is crucial in order to find ways to enhance innate immunological memory and could lead to the development of new vaccines and therapeutics.

## **Study objective**

To elucidate the host and environmental factors that influence the magnitude of the individual trained immunity responses to BCG vaccination using a systems biology approach.

## **Study design**

The intervention trial will be performed at the Radboudumc. 300 Healthy volunteers (equal numbers of females and males) will be recruited to receive a vaccination with BCG. After screening and obtaining informed consent, blood will be drawn by venipuncture before, 2 weeks and 3 months after vaccination. In addition, at these three time points gut and oral microbiome samples will be collected and volunteers are asked to complete a questionnaire.

## **Intervention**

BCG vaccine.

## **Study burden and risks**

BCG vaccine is the most used human vaccine in the world, with an excellent track record of safety.

Potential risks include only the side effects of the vaccine, of which localized skin reactions are most common. The local reaction after BCG vaccination is usually mild and self-limiting. Less common are fever and headache after vaccination and if they occur they are typically mild. Enlargement of the axillary lymph nodes may occasionally occur after vaccination but will usually regress spontaneously after a few months. Local haematoma formation could occur at the site of vena puncture. Both vaccination and vena puncture will only be performed by experienced personnel in this study.

Apart from protection against extrapulmonary infection with *Mycobacterium tuberculosis* and against leprosy, there are no expected benefits for participants in the study. However, findings may show new mechanisms responsible for the non-specific effects of vaccination and this may lead to novel strategies to optimize vaccination programs.

## **Contacts**

### **Public**

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## **Trial sites**

### **Listed location countries**

Netherlands

## **Eligibility criteria**

### **Age**

Adults (18-64 years)

Elderly (65 years and older)

### **Inclusion criteria**

Age>18

Healthy

### **Exclusion criteria**

Use of chronic or acute medication during the last month before the study other than oral anti-contraceptive drugs

Vaccination within 3 months prior to study period

Medical history of disease associated with immune deficiency

Previous BCG vaccination

Contact with tuberculosis patients or born in a tuberculosis endemic country

Acute (febrile) illness within 4 weeks prior to start of study

Pregnancy

## Study design

### Design

**Study type:** Interventional

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Treatment

### Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 10-04-2017

Enrollment: 300

Type: Actual

## Ethics review

Approved WMO

Date: 25-10-2016

Application type: First submission

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date: 24-04-2017

Application type: Amendment

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date: 02-10-2017

Application type: Amendment

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

## 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**

<b>Register</b>	<b>ID</b>
CCMO	NL58553.091.16