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.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immunodeficiency syndromes
Study type	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

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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

Register	ID
CCMO	NL58553.091.16