BCG-induced epigenetic modifications in the NEXT generation

Published: 12-06-2023
Last updated: 21-12-2024

To study the possible epigenetic modifications in sperm cells after BCG vaccination

Ethical review	Approved WMO
Status	Completed
Health condition type	Infections - pathogen unspecified
Study type	Interventional

Summary

ID

NL-OMON53174

Source
ToetsingOnline

Brief title
NEXT

Condition

- Infections - pathogen unspecified

Synonym
Epigenetics; molecules on top of/surrounding DNA

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: spinozapremie

Intervention

Keyword: BCG vaccine, epigenetics, intergenerational

Outcome measures

Primary outcome

The main endpoint is the change in DNA methylation signatures of sperm cells in

the intervention group, from

baseline to 3 and 6 months after BCG vaccination, in comparison to a

placebo-treated group

Secondary outcome

Functional assessment of immune cell populations in both groups, at all

timepoints.

Study description

Background summary

Non-specific protective effects against infections and overall mortality induced by the BCG vaccination have been recently proposed to be inheritable. Since the BCG vaccine is known to induce trained immunity, epigenetic reprogramming of sperm cells might explain the fathers* contribution to the immune profile of their offspring.
Epigenetic inheritance in mice has recently been demonstrated, but is not established in humans yet. By studying the DNA methylation profile of sperm cells after BCG vaccination, we aim to investigate the possibility of cross-generational transmission of resistance to infection in humans through epigenetic reprogramming

Study objective

To study the possible epigenetic modifications in sperm cells after BCG vaccination

Study design

The NEXT study is a single-blind, randomized placebo-controlled trial.
Participants will take part in five study visits

over a period of six months, where samples of blood and sperm cells will be collected.

Intervention

Participants will be randomized 1:1 to receive either a BCG vaccine or a placebo, administered intradermally. After
this intervention, four more study visits will take place to monitor adverse events and collect samples

Study burden and risks

This trial does not include groups that are considered vulnerable. The risks to participants are very low, as the used
vaccine has a well-established safety profile in all age groups, with mainly locally, mild and spontaneously resolving
side-effects. Although venous puncture has some risks (e.g. formation of a hematoma), these are considered
negligible. The amount of blood drawn (300ml in 6 months) is not expected to have any negative consequences.
Collection of sperm cells can be done in the privacy of the participants* own home.
An import detail is that oligo/azoospermia might be discovered. This will be discussed with the concerning participant, but is likely to be burdensome and emotional.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Male
18-25 years old
Healthy

Exclusion criteria

Any systemic disease or condition, or the use of systemic medication
Smoking
Prior BCG vaccination
Other vaccination four weeks prior to trial start or four weeks after the first study visit
Acute illness 2 weeks prior to trial start
Known allergy or anaphylaxis/serious adverse reaction to any vaccine
Participation in another drug trial

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	02-10-2023
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	12-06-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-09-2024
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
ClinicalTrials.gov	NCT05766345
CCMO	NL84471.091.23