Intestinal microbiota and healthy breasts

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON25698

Source
Nationaal Trial Register

Brief title
Intestinal microbiota and healthy breasts

Health condition

Microbiome, Intestinal microbiota, Postmenopausal women without breast cancer, Breast cancer

Sponsors and support

Primary sponsor: Maastricht University Medical Centre (MUMC+)
Source(s) of monetary or material Support: -

Intervention

Outcome measures

Primary outcome

The primary endpoints include the microbiota composition.

Secondary outcome

Secondary endpoints include absolute microbiota abundance and ß-glucuronidase activity.

Study description

Background summary

Background

Intestinal microbiota and host determinants evolve in symbiotic and dependent relationships resulting in a personal ecosystem. In case of dysbiosis, microbiota can instigate cancer development and even change response to systemic cancer treatment. High circulating estrogen levels are recognized as a causal factor for estrogen receptor-positive breast cancer development. Microbiota related estrogen sources are the estrobolome (the aggregate of bacterial genes capable of metabolizing estrogens) and bacterial ß-glucuronidase activity that increases the availability of intestinal estrogen for reabsorption into the bloodstream. Correlations between microbiota related estrogens and systemic estrogen levels are already proven. At this moment, the role of intestinal microbiota in postmenopausal breast cancer treatment is being investigated in Maastricht University Medical Center +. However, there's no knowledge on the intestinal microbiota in postmenopausal women without breast cancer.

Purpose

Investigate the intestinal microbiota composition in postmenopausal women without breast cancer in order to:

1. Gain insight in the intestinal microbiota composition postmenopausal women without breast cancer.

2. Being able to compare the intestinal microbiota composition of postmenopausal women without breast cancer with the microbiota composition of breast cancer patients.

Methods

The intestinal microbiota composition and absolute abundance of the fecal samples will be analyzed with 16S rRNA Next Generation Sequencing (NGS) with subsequent qPCR to convert relative abundance to absolute abundance.

Microbiota analysis

The microbial analysis of the fecal samples will be achieved by 16S rRNA Next Generation Sequencing using the MiSeq platform. Metagenomic DNA from fecal samples will be isolated using a combination of repeated bead-beating and column based purification in accordance with the recommendations of the International Human Microbiota Standards consortium. The V3-V4 hypervariable regions of the 16S rRNA gene will be amplified using bar-coded fusion primers and sequenced using MiSeq 300 PE sequencing (~25,000 reads/sample). This

approach has been proven a powerful tool to provide a complete overview of the diversity and relative abundance of complex microbial communities. Quantitative polymerase chain reaction (qPCR) will be conducted to convert relative abundance to absolute abundance. Although the current project focuses on the taxonomic microbial composition, samples are being properly stored to enable future (functional) metagenomic analyzes.

16S rRNA NGS analysis will be performed when all fecal samples of the ongoing microbiota studies in MUMC+ are collected. This will be approximately in 2020. 16S rRNA NGS analysis should be performed all at once, to avoid batch differences. qPCR analysis could be performed during the inclusion process.

Statistical analysis

For bioinformatic analysis of MiSeq-data, the expandable software package QIIME will be used. After quality filtering and chimera checking, reads are clustered into Operational Taxonomic Units (OTUs) against the Greengenes reference database. For all subsequent analysis, we will normalize the count-table of OTUs using variant stabilization by the R-package DESeq2 13 to account for differences in sequencing depth between the samples. Gut microbiota analysis will include alpha-diversity analysis of OTU richness and evenness within each sample and beta-diversity analysis between samples. For microbial richness and diversity (alpha diversity), the following indices will be calculated: Observed species (richness), Chao1 (estimated richness) and Shannon index (biodiversity).

Functional properties of the microbiota will be inferred using Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (Picrust) and further compared using Statistical Analysis of Metagenomic Profiles (STAMP).” This approach enables the prediction of the estrobolome (abundance of bacterial genes capable of metabolizing estrogen) based upon the bacterial composition.

Multivariate analysis will be used for the classification of bacterial and postmenopausal women with and without breast cancer. Multivariate analysis will be used to correlate specific bacterial composition, abundance (estrobolome) and ßglucuronidase activity with postmenopausal women with and without breast cancer.

Study objective

1. The intestinal microbiota composition of postmenopausal women without breast cancer differs from breast cancer patients.

2. The estrobolome and bacterial ß-glucuronidase activity will be less abundant in postmenopausal women without breast cancer compared to postmenopausal breast cancer patients.

Study design

One fecal sample and one questionnaire will be collected within 8 weeks after the mammography.

Intervention

An observational study at the Dutch Screening for Breast Cancer will be performed in 66 postmenopausal women without breast cancer. By acquiring insight into the intestinal microbiota composition of postmenopausal women without breast cancer, a control group will be set up for already existing research lines in microbiota research in breast cancer patients at MUMC+. Fecal samples and questionnaires will be collected. The intestinal microbiota composition and absolute abundance of the fecal samples will be analyzed by with 16S rRNA Next Generation Sequencing (NGS) with subsequent qPCR to convert relative abundance to absolute abundance.

Contacts

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Eligibility criteria

Inclusion criteria

• Postmenopausal women without breast cancer following the National Dutch Screening for Breast Cancer in Maastricht

Exclusion criteria

• Mammography older than 8 weeks prior to fecal sample collection.

• Any type of cancer in history

• Inflammatory Bowel Disease

• Therapeutic antibiotic use 3 months prior to fecal sample collection

• Physically or mentally incapable or incompetent to sign informed consent

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other

Control: N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-09-2018
Enrollment:	66
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	17-09-2018
Application type:	First submission

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
NTR-new	NL7256
NTR-old	NTR7478
Other	METC 17-4-075, METC 172016 : METC 2018-0688

Study results