COLLECTION OF DNA AND RNA FROM BREAST CANCER PATIENTS

Published: 29-09-2010
Last updated: 30-04-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Observational invasive

Summary

ID

NL-OMON34596

Source
ToetsingOnline

Brief title
Breast Cancer Genome Analysis

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: breast cancer, DNA, genome analysis, RNA

Outcome measures

Primary outcome

Primary outcome measures will be the generation of comprehensive catalogues of

genomic abnormalities for a minimum

of 500 breast cancer samples by sequencing to high coverage depth both the

cancer and matching normal genomes

which will include identification of single nucleotide variants, insertions,

deletions, copy number changes, translocations

and other chromosomal rearrangements in conjunction with the generation of

transcriptomic and epigenomic data sets

using state*of*the*art approaches, such that most cancer genes mutated at 3% or

greater prevalence will be identified.

Secondary outcome

none

Study description

Background summary

All cancers arise due to accumulation of damage in genetic material which affects critical target genes. Altering the
function of these critical genes affects growth control in cells resulting in what is clinically recognised as cancer.
Identifying the specific abnormalities and genes associated with a particular cancer allows a greater understanding of the
causation of the cancer and potentially provides targets for diagnostic investigations and novel anti*cancer therapies.

Important examples of the latter include Herceptin in breast cancer, Gleevec in chronic myelogenous leukemia and
Iressa/Tarceva in non*small cell lung cancers.
The Cancer Genome Project at the Sanger Institute was established to undertake systematic genomic analyses of cancers
in order to identify of new cancer genes. Subsequently, there has been a major effort to organise and coordinate
international efforts by establishment of the the International Cancer Genome Consortium, whose goal is to more fully
investigate the many different types of human cancer * ultimately leading to complete cataloguing of all genetic events that
are important in the cancer. These data will be the foundation for further efforts focused on improving prevention,
diagnosis and treatment informed by detailed molecular knowledge of the key events contributing to each tumour type.
Following the completion of the human genome reference sequence, the possibility of using systematic genome wide
screens to help understand the mechanisms of cancer development and biology is now a realistic goal. As a result the
International Cancer Genome Consortium was launched to maximise the impact and aid co*ordination of such studies.
The principle aim of this study is to characterise all of the genetic alterations that are present in different types of breast
cancer by comparing the cancer genome to it's matched normal genome.
Somatic mutations refer to changes in the DNA sequence of an individual's cells that occur during normal life. They are
not inherited from parents or passed onto offspring. However, if one or more of these changes takes place within or affect
a particular type of gene (known as a cancer gene) then the cell that has acquired the change will proceed to become a
cancer cell. Understanding the critical mutational events underlying the development of cancer is paramount for
advancing prevention, early detection and effective treatment of the disease.
Proteins in the body are not made from DNA directly. An edited version of DNA is produced which is known as RNA.
The process of making RNA is termed transcription and the RNA acts as the intermediate between DNA and the rest of
the cell. The transcriptome is the complete set of RNA products that are produced by the genome. Transcriptomics
refers to the study of these RNA products. Epigenetic processes control normal growth and development by activating or
deactivating certain genes within a cell. Epigenomic data sets will provide information relating to any changes in those
processes across many genes or an entire organism.
Study of the whole genome to identify mutational changes which may influence or give rise to the development of cancer
will include in*depth sequencing of DNA as well as studying the transcriptomes

and epigenomes to understand the
processes occuring in tumour cells when compared to normal cells.

Study objective

The principle aim of this study is to characterise all of the genetic
alterations that are present in different types of breast
cancer by comparing the cancer genome to it's matched normal genome.The primary goals of this ICGC project, which focuses on breast cancer, are:
1) Co*ordinated generation of comprehensive catalogues of genomic abnormalities (somatic mutations) in breast cancer
to include single*nucleotide variants, insertions, deletions, copy number
changes, translocations and other chromosomal
rearrangements by sequencing of cancer and matching normal genomes to high levels of coverage.
2) Generate complementary catalogues of transcriptomic and epigenomic data sets from the same tumours.
(Some of this work may be carried out by one or more of the international
partners in the Breast Cancer Working Group
and not necessarily at the Sanger Institute).
3) Release the data to the research community as rapidly as possible and, where appropriate, with minimal restrictions to
accelerate research into the causes and control of cancer.

Study design

Purpose:
To identify the full range of genomic abnormalities that can lead to the development of cancer.
Design:
From the tissues removed from participants for routine diagnostic purposes as part of their clinical care, DNA and RNA will
be extracted. At the point of clinical care, a microfine section of the tissue that has been removed will be used to create a microscopic slide for review by pathologists. These slides will also be made available for this study and as such may be stored at the Wellcome Trust Sanger Institute for a period of time.
Tumour DNA will be analysed and compared to matching constitutional (normal) DNA from the same patient to identify
tumour*acquired (somatic) alterations. These alterations (mutations, copy number alterations, translocations and other
genomic aberrations) will be identified in multiple tumours and then these sets compared against each other to determine
which genes are mutated in common and which pathways have been targeted. A combination of DNA sequencing,
methylation, epigenetic and microarray*based methods will be used in these analyses.

The sequencing will consist of next*generation deep sequencing of the tumour nucleic acids at the Wellcome Trust
Sanger Insitute which will identify the variants present in the tumour down to single nucleotide resolution. It is possible that
a subset of sequencing maybe carried out at Illumina, Inc based at Great Chesterford, Cambridge. In additional, normal
DNA extracted from blood (or other non*cancerous tissue biopsy samples) will be sequenced at sufficient coverage to
allow true somatic variants to be initially identified and separated from previously undescribed population polymorphisms.
Reconfirmation of novel somatic variants (i.e. those present in the tumour but not the normal DNA) will be conducted by
resequencing of the specific regions

Study burden and risks

not applicable

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

Participants have a confirmed diagnosis of breast cancer (any subtype).

Exclusion criteria

see inclusion

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-11-2010
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO

Date:	29-09-2010
Application type:	First submission

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	NL32596.091.10