The biology of ageing in relation to acute myeloid leukemia (AML) in older patients

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The aim of the study is to:1. Attain more insight in the biology of ageing of hematopoietic stem cells2. Attain more insight in the relation between ageing and cancer

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Observational invasive

Summary

ID

NL-OMON39102

Source
ToetsingOnline

Brief title
Ageing of the hematopoietic system

Condition

- Leukaemias

Synonym
AML

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: KWF Kankerbestrijding (RUG 2009-4566)

Intervention

Keyword: - ageing, - AML, haematopoietic stem cells

Outcome measures

Primary outcome

We aim to identify molecular pathways which are activated upon ageing to protect stem cells against damage but are down-regulated in AML cells of older patients.

Secondary outcome

We aim to explore whether oncogenic hits have different molecular and cellular consequences depending on the age of the target cell.

Study description

Background summary

Acute myeloid leukemia (AML) is a malignant blood disorder. AML occurs in all ages, but mainly in elderly patients (>60 years). The last decade a lot of progress has been made in the treatment results. However, only patients younger than 60 years have benefited. Because of differences in clinical characteristics (eg inherent chemotherapy resistance) and biological characteristics (eg the occurence of complex aberrant karyotypes) in AML in elderly patients, AML in elderly is considered to be a different disease. The lack of molecular data to explain these differences between AML in elderly and AML in younger patients, has motivated us to compare gene expression profiles of AML cells of young and elderly patients. This research showed that there are indeed molecular (= gene expression) differences between AML cells of younger and elderly patients. A striking gene was p16, which expression was lower in AML cells of elderly patients, while during normal ageing of healthy hematopoietic stem cells the expression increases with age. It is even pressumed that the higher expression of p16 during ageing plays an important role to 'expand' damaged stem cells so that these cannot cause a malignant disease anymore. As a result the number of functional stem cells decreases as well as regeneration capacity of the different tissues. So the higher expression of p16 during ageing protects us from cancer, caused by accumulation of DNA damage and proteins during ageing, with ageing as a result. From this perspective the lower expression of p16 in AML cells of elderly patients with respect to younger patients, suggests that the elimination of mechanisms that protect us from accumulation of DNA damage (such as higher expression of p16), are necessary to develop leukemia in old stem cells.

The aim of this study is to attain more insight in the relation between ageing and cancer. In the first place we want to compose a list of genes, besides p16, that play a specific role in the development of AML in elderly patients. In subsequent experiments we wil show the biological interest of these genes in CD34+ healthy and AML cells. Further, we would like to understand why the introduction of a certain oncogene in a young stem cell has other consequences than the introduction of this oncogene in an old stem cell. Technically we can achieve this by infecting old and young hematological stem/precursor cells with viruses containing a certain cancer gene.

Study objective

The aim of the study is to:
1. Attain more insight in the biology of ageing of hematopoietic stem cells
2. Attain more insight in the relation between ageing and cancer

Study design

See chapter 4 and 5 protocol.

Study burden and risks

Risks for participants in this study are:
1. For older individuals undergoing a total hip replacement the surgery will be a few minutes delayed.
2. For volunteers younger than 35 years of age and the healthy potential donors no risks are expected.
3. Bleeding due to bone marrow aspirate is NOT an expected problem

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

- a doctor's diagnosis of normal general health
- not suffer from a hematological disease
- people older than 60 years of age who get a total hip replacement
- healthy volunteer < 35 years
- heatlhy potential donor who undergoes a routine bone marrow aspirate as part of the standard medical examination

Exclusion criteria

- patients suffering from a hematological disease

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2010
Enrollment:	75
Type:	Actual

Ethics review

Approved WMO Date:	24-11-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-02-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL32763.042.10