Quantification of leukocyte dynamics in bone marrow of healthy humans

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To quantify leukocyte turnover, characterize immune phenotype and function, determine T-cell receptor repertoire, and measure soluble immune factors in bone marrow and blood of healthy adults.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	White blood cell disorders
Study type	Observational invasive

Summary

ID

NL-OMON56359

Source
ToetsingOnline

Brief title
DYNAMO (leukocyte DYNAmics in huMan bOne marrow (DYNAMO)

Condition

- White blood cell disorders

Synonym
immunological memory, maintenance of immune cells

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: NWO

Intervention

Keyword: bonemarrow, deuterated, leukocyte, quantification

Outcome measures

Primary outcome

The average turnover of different immune cell subsets in bone marrow of healthy human adults during homeostasis.

Secondary outcome

- The average turnover and lifespan of antigen-specific T cell subsets in bone marrow and paired blood;

- The phenotype of immune cells in bone marrow and paired blood based on flow cytometric markers (percentage positive and mean fluorescence intensity).

- The function of immune cells in bone marrow and paired blood based on in vitro stimulation assays, e.g. in IFN-g or TNF-a production.

- Concentration of factors in plasma and bone marrow and paired blood that can influence leukocyte dynamics, such as growth and survival factors, infection parameters, and viral factors.

- Comparison of the T-cell receptor (TCR) repertoire between blood and bone marrow;

- Determination of the phenotype of adaptive NK cells in blood and bone marrow using scATAC-seq.

Study description

Background summary

Most insights into human immune cells have been based on cells isolated from the blood. There are strong indications, however, that the bone marrow provides a special niche for immune cells. It is the place where many leukocytes find their origin, and it has been suggested that antigen-experienced T- and B-cells in the bone marrow are protected from death and thereby retain long-term immunological memory. In this research, we want to investigate the lifespan of leukocytes in bone marrow of healthy adults and gain insight in the differences between leukocytes in peripheral blood versus bone marrow.

Study objective

To quantify leukocyte turnover, characterize immune phenotype and function, determine T-cell receptor repertoire, and measure soluble immune factors in bone marrow and blood of healthy adults.

Study design

Investigator-driven, multicentre, longitudinal, non-interventional, pilot study with invasive procedures and imposed rules of conduct.

Study burden and risks

Participants will drink heavy water for a maximum of 9 weeks. They will also donate bone marrow after a study-independent hip or knee replacement surgery, undergo 1-5 venepunctures, and collect multiple saliva/urine samples. The risks related to deuterated water intake, venepuncture, and saliva/urine donation are low. Collection of bone marrow (rest material) after the hip or knee replacement surgery does not add additional risks to the already scheduled elective surgery. Even though the physical burden and risks of this study are minimal, the personal burden is higher: participants will have to invest time and energy to visit the hospital, donate blood, saliva/urine, and bone marrow, and drink daily heavy water at home. There is no direct benefit in participation and the risks are minimal.

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

Elective hip or knee replacement surgery, older than 55 years of age

Exclusion criteria

(Pathological) fracture as surgery indication, chronic infection, daily use of immuno-modulatory drugs

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):	08-12-2021
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	11-03-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	23-11-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL74992.041.20