Neutrophil and macrophage extracellular trap formation

Published: 15-05-2024
Last updated: 29-05-2024

-To investigate the development of ETs through the role of platelets and activated endothelium by performing co-culture experiments with neutrophils, macrophages, platelets and renal-derived endothelial cells. -To determine whether deceased donor...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON56756

Source
ToetsingOnline

Brief title
Neutrophil and macrophage extracellular trap formation

Condition

- Other condition

Synonym
kidney transplantation

Health condition

transplantatie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: extracellular traps, macrophages, neutrophils, transplantation

Outcome measures

Primary outcome

Quantification of extracellular traps formed in the supernatant of co-culture

experiments of isolated neutrophils, macrophages, platelets and endothelial

cells.

Secondary outcome

not applicable

Study description

Background summary

Kidney grafts from deceased donors have inferior quality compared to grafts from living donors. A large percentage of transplanted grafts are however from deceased donors. Thus, finding strategies to improve the quality of organs from deceased donors is crucial. During brain or circulatory death, the pro-inflammatory environment primes the activation of various immune cells and accordingly, increased leukocyte infiltration has been shown in grafts from brain and circulatory dead donors. Neutrophils and macrophages can release extracellular traps (ETS), a specific form of nuclear membrane disintegration or blebbing that results in the release of chromatin, DNA and cytoplasmic granules to the extracellular environment in response to specific stimuli. These cells might therefore be involved in the tissue damage observed in deceased donor grafts through the specific pathway of ET formation. During brain or circulatory death, the endothelium is activated, while activated platelets infiltrate grafts to participate in the formation microthrombi. It is hypothesised that activated platelets and endothelial cells might be involved in mediating the release ETs in deceased donor grafts. The project therefore aims to determine whether the formation of ETs in grafts from deceased donors

are mediated by platelet and endothelial cell activation. In vitro assays with isolated neutrophils, macrophages, platelets, and cultured endothelial cells from kidney grafts or human umbilical cord endothelial cells stimulated with pro-inflammatory cytokines will be performed to determine whether platelets and the endothelium are mechanistically involved in ET formation. Knowledge gained through the project could contribute to strategies aimed at improving the quality of kidneys from deceased donors in a clinical setting.

Study objective

-To investigate the development of ETs through the role of platelets and activated endothelium by performing co-culture experiments with neutrophils, macrophages, platelets and renal-derived endothelial cells.
-To determine whether deceased donor plasma stimulates ET release in isolated neutrophils or macrophages.

Study design

In-vitro study

Study burden and risks

Participation in the study will involve the draw of a blood sample [20 millilitres (mL)] by a qualified medical practitioner at the UMCG during two visits. Phlebotomy is normally done as part of routine medical care but may present a slight risk and discomfort. This may result in a bruise at the puncture site, or less commonly swelling of the vein, infection and bleeding from the site.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthy human volunteers, over 18 yr old
Informed consent obtained

Exclusion criteria

* Smoking
* Use of chronic medication
* The use of any medication known to alter platelet function within the last ten days prior to blood being drawn (i.e., Aspirin)
* The presence of any chronic or inflammatory diseases e.g. tuberculosis, rheumatoid arthritis or hepatitis A, type 1 or 2 diabetes mellitus, inflammatory bowel disease etc.
* Recent or heavy alcohol consumption (in the last 24 hours or *15 drinks/week)
* In females, pregnancy, the use of oral contraceptives or hormone replacement therapy
* BMI above a normal range

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Other

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-12-2023
Enrollment:	12
Type:	Anticipated

Ethics review

Approved WMO

Date:	15-05-2024
Application type:	First submission
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	NL84552.042.23