In vitro investigation into the potential regulating role of sphingolipids in lymphocyte proliferation.

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

Summary

ID

NL-OMON40165

Source
ToetsingOnline

Brief title
Role of sphingolipids in lymphocyte function

Condition

- White blood cell disorders
- Autoimmune disorders

Synonym
not applicable

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: ABC-transporter, lymphocyte, Sphingosine

Outcome measures

Primary outcome

The main study parameter is the in vitro proliferation rate of lymphocytes, measured as the number of cells, after 72 hours of incubation with specific agonists or antagonists for the sphingosine-receptors and substrates or blockers of the sphingosine-kinase and -transporter (i.e. the ABC C1-transporter).

Secondary outcome

Not applicable.

Study description

Background summary

Sphingosine-1-phosphate (S1P) is a bioactive lipid involved in a wide range of cellular processes, such as cell migration, differentiation and protection from apoptosis. S1P has both extracellular effects through five G-coupled receptors (S1PR1-5) as well as intracellular effects by interactions with target proteins. Lymphocytes have important functions in specificity, diversity, self-tolerance and immunological memory. The egress and recirculation of lymphocytes from thymus and secondary lymphoid organs depends on the S1PR1 receptor. Release of T-cells from the thymus and the interaction between T- and B-lymphocytes in secondary lymphoid organs is essential for the functioning of the adaptive immune system. Activation of S1PR1 on the lymphocyte membrane leads to lymphopenia, probably due to sequestration of lymphocytes in secondary lymphoid organs, while entering into lymphoid organs depends on loss of S1PR1 due to internalization. Since activation of S1PR1 leads to lymphopenia, development of S1P agonists seems promising for immunosuppressive therapy in transplantation medicine and autoimmune disease.

Study objective

More sustained knowledge of the intracellular processes regarding S1P in lymphocytes could be beneficial in modulating specific immune responses in transplantation medicine, autoimmune diseases and sepsis. Therefore, in this study, we will investigate S1P induced lymphocyte proliferation and its underlying cellular mechanisms.

Study design

In vitro met vers geïsoleerde lymfocyten . in vitro eindpunten zijn de vaststelling van een merkbare verandering van de proliferatiesnelheid van de lymfocyten gedurende 72 uur in aanwezigheid of afwezigheid van specifieke agonisten of antagonisten voor de receptoren en sfingosine - substraten of remmers van de sfingosine - kinase en - transporter (de ABC C1 - transporter) . Derhalve zal het aantal cellen schatting door het meten van fluorescentie signaalintensiteit via de NF celproliferatie Assay Kit (Invitrogen Molecular Probes , Oregon , USA) . De gemeten fluorescentiesignaal is een continue variabele die wordt gebruikt als een surrogaat voor het aantal cellen in het experiment . Statistisch verschil wordt berekend met behulp van T - toets van de student voor onafhankelijke monsters (in het geval waarin twee groepen vergeleken worden) of een One - Way ANOVA met post - hoc Games - Howell (in het geval waarin drie of meer groepen zijn vergeleken) . Gegevens zullen worden geanalyseerd met behulp van de meest recente beschikbare versie van SPSS voor Windows -werkstation

Study burden and risks

The study poses a negligible risk for the volunteer, as the only intervention will be drawing of blood at one single occasion. Increasing our fundamental knowledge about the regulating role of sphingolipids on lymphocyte proliferation might lead to the discovery of novel targets for pharmacological intervention that will allow modulation of lymphocyte function. The results could contribute to a better understanding of cellular mechanisms in adaptive immunity which potentially allow targeted immunomodulation in transplantation medicine, autoimmune diseases and sepsis.

Contacts

Public
Universitair Medisch Centrum Groningen

Antonius Deusinglaan 1
Ggroningen 9713 AV
NL
Scientific

Universitair Medisch Centrum Groningen

Antonius Deusinglaan 1
Ggroningen 9713 AV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must be at the age between 18 and 65 years old.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study: clinically relevant infection or inflammation, malignancy, any systemic disease, pregnancy.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-03-2014
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	19-02-2014
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	NL46926.042.13