# The Red Blood Cell in Patients with Neuroacanthocytosis: an explorative study on regulation of morphology and function of red blood cells of patients with neurodegeneration of the basal ganglia.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Red blood cell disorders
Study type	Observational invasive

# Summary

### ID

NL-OMON38521

**Source** ToetsingOnline

Brief title RBC-EMINA

# Condition

- Red blood cell disorders
- Structural brain disorders

### Synonym

neuroacanthocytosis; choreoacanthocytosis

# **Research involving**

Human

### **Sponsors and support**

**Primary sponsor:** Universitair Medisch Centrum Sint Radboud **Source(s) of monetary or material Support:** EU via ZONMW

### Intervention

Keyword: neurodegeneration, red blood cell, signaling

### **Outcome measures**

#### **Primary outcome**

The main study parameters are characteristics of red blood cell structure and

function in vitro:

- A. deformability in capillary flow conditions.
- B. deformability in spleen-like conditions.
- C. cell morphology.
- D. cell membrane composition.
- E. metabolic status.
- F. characteristics and kinetics of erythropoiesis in vitro.
- G. active signaling pathways.

#### Secondary outcome

na

# **Study description**

#### **Background summary**

In recent years, there has been an increasing awareness in the biomedical community that function and survival of the red blood cell are finely tuned and

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regulated processes [1]. This insight has been parallelled by the development and application of new tools for the study of red blood cell physiology. Intricately interwoven with these studies, it has become clear that red blood cells are involved in various systemic diseases, such as diabetes, iron accumulation, and inflammation [2-4]. Also, the ready availability of red blood cells is an important advantage compared with that of cells from all organs, in particular the brain.

The composition of the red blood cell membrane is one of the best known in modern cell biology, but the molecular mechanisms of the (regulation of the) interaction between lipid bilayer and cytoskeleton are far from understood. The effects of disturbance of this interaction on cell morphology, deformability and survival have, so far, mostly been deduced from red blood cell-centered genetic diseases such as sickle cell disease and other \*membranopathies\* [5]. Relatively little is known on the regulation of physiological aging and removal, and even less on the effects of disturbance of these processes on the homeostasis of the whole organism. Recent data from proteomic and metabolomic studies strongly suggest that red blood cells have a functional interaction with soluble and cellular components of the circulation, such as cytokines, lipids, endothelial cells, and immune cells [6, 7]. Such data also indicate that elucidation of the mechanisms underlying abnormal red blood cell shape may be instrumental in understanding the pathopysiology of other cells, including degenerating neurons in the basal ganglia [8].

Thus, there is an urgent need to identify the molecular mechanisms that regulate function and survival of the red blood cell in health and disease. More specifically, molecular identification of the mechanism leading to the formation of acanthocytes has, so far, been the only way to study the pathobiology of neuroacanthocytosis (chorea-acanthocytosis, McLeod disease, Huntington disease-like II, neurodegeneration with brain iron accumulation) affecting the basal ganglia [9].

### **Study objective**

The main, primary objective of this study is identification of the molecular mechanisms that regulate structure and function of red blood cells in patients with neurodegeneration accompanied by the presence of abnormal red blood cells (neuroacanthocytosis). Hereto, selected characteristics of the red blood cells of patients will be compared to those of healthy donors, before or after experimental manipulation in vitro (see als the section 'primary study parameters').

Secondary objectives are: (1) an understanding of the mechanism of neurodegeneration in patients with neuroacanthocytosis; (2) the development of biomarkers for diagnosis and disease progression.

The first step towards these objectives is an inventory of the molecular

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characteristics of the red blood cells of patients with neuroacanthocytosis, in comparison with those of healthy donors.

#### Study design

Our study will be an explorative, observational study, consisting of a comparison of structure and function of red blood cells of patients with neuroacanthocytosis with those of healthy, age-matched and gender-matched control donors in vitro.

The duration of the study is five years; the setting of the study is within one of the research lines of the Department of Biochemistry, Radboud University Medical Centre: \*The Red Blood Cell in Health and Disease\* and the E-RARE/ZONMW project \*Advancing the European Multidisciplinary Initiative on Neuroacanthocytosis EMINA-2: dissecting the molecular pathophysiology of chorea-acanthocytosis // Signalling cascades involved in neuronal and erythrocyte dysfunction in ChAc\*.

#### Study burden and risks

The only burden and risks associated with this study are those that are associated with a venipuncture of 5-15 ml blood by qualified personnel, identical to the procedure that is used for routine diagnostic purposes.

# Contacts

#### Public

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# **Trial sites**

# **Listed location countries**

Netherlands

# **Eligibility criteria**

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

# **Inclusion criteria**

control donors: healthy, 18-55 years old patients: clinical diagnosis neuroacanthocytosis

# **Exclusion criteria**

controls: use of medication with a known effect on red blood cells structure and/or function patients: inability to obtain sufficient data for a clinical diagnosis

# Study design

### Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

### Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	01-09-2013
Enrollment:	30

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Type:

Anticipated

Ethics review	
Approved WMO Date:	30-01-2014
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 CCMO

**ID** NL45934.091.13