Target Molecules and their Respective Pathogenic and Protective Antibodies in Myasthenia Gravis.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON36848

Source
ToetsingOnline

Brief title
Target Molecules in MG

Condition

- Autoimmune disorders
- Muscle disorders
- Neuromuscular disorders

Synonym
Myasthenia Gravis

Research involving
Human

Sponsors and support

Primary sponsor: Neurologie

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: antibodies, cell lines, myasthenia gravis

Outcome measures

Primary outcome

The production of 6 monoclonal antibody producing cell lines. The antibodies

produced by this cell line will be used for the identification of new

autoantigens and the development of new neuroprotective antibodies.

Secondary outcome

not applicable

Study description

Background summary

Antibodies are becoming increasingly important agents both as a diagnostic tool as well as therapeutic agents for human diseases. There is accumulating evidence that autoreactive antibodies play key roles in neurodegenerative diseases such as multiple sclerosis, Alzheimer*s disease, schizophrenia and Parkinson*s Disease. However, so far these antibodies have only been poorly characterised and in many diseases the autoantigens remain unknown. Presently, myasthenia gravis (MG) is the best characterised antibody mediated disease and we have cloned and produced one of the few recombinant human autoantibodies. A technique published by Traggiai et al. in 2004 now tremendously simplifies human B-cell cloning, therefore facilitating a broad range of new applications.

Study objective

The aim of this study is to develop an immortalised B-cell line derived from MG patients.
This antibody producing cell line will be used for different applications:
- The establishment of new passive transfer disease models for MG
- The identification of new autoantigens
- The development of neuroprotective antibodies

Study design

The goal of this study is to produce 6 B-cell producing cell lines which will be used for the applications as described above in objectives. To reach this goal we need 2 groups of donors of human material.
The first group of tissue donors consists of 30 MG patients undergoing a thymectomy (robot-thymectomy with the Da Vinci robot according to standard procedures). These patients will be asked to donate a part of the removed thymus gland (2.5 x 2.5 cm), a muscle biopsy of an intercostal muscle (0,5 x 0,5 cm; taken during the operation) and blood (two tubes of 10 ml; collected during the operation). From the thymus tissue B-cells will be isolated for creating an immortalised cell line that will be used for the development of neuroprotective antibodies. The muscle biopsies will be used to study the disease specific changes at the neuromuscular endplate and to study the binding of pathogenic antibodies to affected muscle tissue. The blood will be used for isolation of lymphocytes, which will be studied and used for co-culturing together with the isolated B-cells.
The second group of tissue donors consists of 30 control patients undergoing another type of thoracic operation with the Da Vinci robot for a disorder that is not related to MG, another autoimmune disease, or another disease affecting the muscles, and will not get a thymectomy. These patients will be asked to donate a muscle biopsy only. The muscle biopsy (0,5 x 0,5 cm of an intercostal muscle) will be taken during the operation and will be used to study the neuromuscular endplate of unaffected muscle tissue, the binding of pathogenic antibodies to unaffected muscle tissue, to identify new autoantigens, and to verify that eventually newly developed neuroprotective antibodies do not bind to muscle tissue.

Study burden and risks

The thymectomy in MG patients is part of their regular treatment and will be beneficial to them. Using the wasted material for this study will not change the burden nor the risk for these patients.
Taking muscle biopsies (5 by 5 mm) from patients during an operation will result in a negligible risk with minimal burden. The biopsy will be taken at the place where, as part of the standard operation, a troquart (with a diameter of 12 mm) is inserted in the intercostal space. An incision of the skin and intercostal muscle is already made as part of the operation, so no extra incision is made for the biopsy. As this is an open biopsy the risk is negligible. Any eventual bleeding can be treated immediately.
As the blood sample of 20 ml will be taken from the venflon that is already in place during the operation, the risk and burden are negligible.
The patients will not benefit from participating in this study.

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

age: 18 years and older
For patients with MG: scheduled for a thymectomie using the Da Vinci Robot
For control patients: scheduled for a thoracic operation using the Da Vinci Robot for a disorder that is not related to an autoimmune disease or disease affecting the muscles

Exclusion criteria

minors or incapacitated persons
not willing to give informed consent

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:	Recruiting
Start date (anticipated):	01-08-2008
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	28-07-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	29-10-2008
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	13-08-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	11-07-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL22271.068.08