Scleroderma target discovery

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

Summary

ID

NL-OMON41288

Source
ToetsingOnline

Brief title
Scleroderma target discovery

Condition

- Autoimmune disorders
- Connective tissue disorders (excl congenital)
- Skin vascular abnormalities

Synonym
Scleroderma

Research involving
Human

Sponsors and support

Primary sponsor: BioFocus
Source(s) of monetary or material Support: BioFocus

Intervention

Keyword: Scleroderma, Skin fibroblasts, Target discovery

Outcome measures

Primary outcome

Genes that upon knockdown interfere with SSc-related phenotypes in human

fibroblasts

Secondary outcome

Nvt

Study description

Background summary

Systemic sclerosis (SSc), is a chronic systemic autoimmune disease characterized by fibrosis, vascular alterations, and the presence of auto-antibodies. This disease is found worldwide with women four times more likely to develop scleroderma than men. In the Netherlands, approximately 9 persons in 100,000 persons is affected. SSc is classified according to the American College of Rheumatology (ACR) or LeRoy criteria of early SSc. The prognosis is relatively good for LcSSc patients but is worse for those with the DcSSc, particularly in older age, and for males. Death occurs most often from pulmonary, heart, and kidney complications. Typical SSc is classically defined as symmetrical skin thickening, with about 90% of cases also presenting with Raynaud's phenomenon, nail-fold capillary changes, and anti-nuclear antibodies. Auto-antibodies are important diagnostic tools that can also provide information about the clinical subset of SSc; anti-topoisomerase antibodies, like anti-scl70 most often are present in DcSSc, whereas anti-centromere antibodies are more often observed in LcSSc. Other auto-antibodies can be found as well, such as anti-U3 or anti-RNA polymerase. The events initiating SSc are unknown. Although SSc runs in families, disease-related genes have not been identified yet.

Study objective

Because the pathophysiology of SSc is unknown, there is currently no treatment available to cure the disease itself, so only individual organ system complications are treated (7,8). Therefore, treatment is patient-specific and

aimed at ameliorating symptoms of the disease. This project aims to identify genes that upon knockdown interfere with SSc-related phenotypes in relevant human cells. These targets should be amenable for drug discovery and development, and inhibit or resolve fibrosis in SSc.

Study design

The ultimate goal is to identify targets that, upon knockdown, interfere with SSc-related phenotypes in human fibroblasts by a high throughput shRNA SilenceSelect®library with 16.800 shRNA targeting ~5.250 genes by Biofocus. These targets should be amenable for drug discovery and development, and inhibit or resolve fibrosis in SSc.

Study burden and risks

Skin biopsies are easily mastered, quick and have a low incidence of infection, bleeding, non-healing or significant scarring. Blood sampling will occur at the *Prikpost* B4. Therefore, the risks of this study is limited to a minimal bruise. The participants do not benefit from 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

- Diagnosed with diffuse cutaneous systemic scleroderma according to ACR, Leroy criteria or ACR/EULAR criteria.
- Duration should be equal or less than 18 months since the first non-Raynaud symptom
- Presence of autoantibodies against RNA polymerase III, topoisomerase (Scl-70), antifibrillarine or PMScl.
- Preferably diagnosed recently and no/limited confounding effect of immunosuppressive therapy

Exclusion criteria

- Individuals who fail to meet the inclusion criteria.

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:	Recruitment stopped
Start date (anticipated):	02-01-2014
Enrollment:	20

Type:	Actual

Ethics review

Approved WMO Date:	04-11-2013
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-06-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL46199.058.13