Mesenchymal stem cells in emphysema

No registrations found.

Ethical review	Not applicable
Status	Other
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON21186

Source
NTR

Health condition

COPD, Emphysema, mesenchymal stem cells

Sponsors and support

Primary sponsor: Pathology & Medical Biology and Pulmonology Dept., University Medical Center Groningen
Source(s) of monetary or material Support: Longfonds, Stationsplein 127, 3818 LE Amersfoort

Intervention

Outcome measures

Primary outcome

1. Succesfull isolation and culturing of mesenchymal stemcells derived from lung tissue.

2. Succesfull isolation and culture of mesenchymal stemcells derived from adipose tissue.

Secondary outcome

1. Analyses of differential MSC function between COPD and control groups through RTPCR, immunohistochemical stainings and Western Blot.

Study description

Background summary

Emphysema is a prevalent chronic lung disorder associated with chronic inflammation and irreversible alveolar damage. Currently, there is no cure for emphysema. Novel therapeutic strategies are needed, including regenerative approaches using stem cells and bioactive scaffolds. Recent studies indicate that especially the use of mesenchymal stem cells (MSCs) is promising. MSCs produce antiinflammatory factors and display regenerative capacity, constituting a niche for alveolar repair by the production of growth factors and structural proteins. Animal studies indicate that delivery of autologous lungderived MSCs can reduce alveolar damage. Still, the challenge of regenerative medicine in emphysema is considerable. The reparative capacity of MSCs from emphysema patients may be deficient, due to an increased oxidative stress burden and/or dysregulation of lung developmental pathways, as corroborated by preliminary data. Additionally, preliminary data support the notion that there is extensive loss of extracellular matrix (ECM) in emphysema, hampering MSC engraftment and activity.
We hypothesize that these abnormalities underlie the defective repair in emphysematous lungs. The use of a bioactive scaffold potentially promotes MSC engraftment, tissue persistence and regenerative capacity, although knowledge on the optimal composition of such a scaffold is limited.

In this obesrvational study we will pay attention to:

· Feasibility to derive MSCs from bronchial biopsies, lung tissue resection material, and adipose tissue,

· Ability of isolated MSCs to self-renew and differentiate,

· Ability of isolated MSCs to expand and express growth factors, anti-inflammatory mediators, cell surface receptors and ECM proteins upon culture,

· Improvement of the regenerative capacity of MSCs by the use of effector molecules, e.g. WNT proteins and IL-1R antagonists,

· ECM composition of decellularized human lungs at different levels of the bronchoalveolar tree,

· Engraftment, cell survival and growth factor expression of MSCs seeded on decellularized human lung slices,

· Construction of 3D-scaffolds, mimicking the structure of the normal lung, using different composition of ECM molecules and growth factors,

· Bio-scaffold composition that creates an optimal micro-environment that sustains MSC survival and function,

· Effects of MSCs on epithelial function, e.g. epithelial barrier function, repair, mitochondrial function and differentiation into alveolosphere-like structures using Matrigel.

Study design

All tissue will be collected during the planned interventions, with no additional time points planned.

Intervention

1. Central bronchial biopsies of the 1st, 3rd and 5th generation will be taken from 20 emphysema patients admitted to the bronchoscopic lung volume reduction program in the UMCG.

2. Lung resection material will be obtained from COPD patients and nonCOPD controls, who undergo lung transplantation or lobectomy / pneumectomy because of lung cancer.

3. Lung cancer patients who undergo lobectomy / pneumectomy will be selected on basis of the size and location of the tumor, enabling adequate collection without interfering with routine oncopathology procedures.

4. Adipose tissue (1cm3) will be obtained during the same

lung resection procedures described in points 2 and 3.

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Eligibility criteria

Inclusion criteria

Lung resection material will be obtained from
COPD patients and nonCOPD
controls, who undergo
lung transplantation or lobectomy / pneumectomy because of
lung cancer. COPD patients will be selected on
basis of having smoked more than 20 pack years and having
clinical signs of emphysema. Written informed consent will be
collected from all patients in order to be eligible for inclusion.
The nonCOPD
controls will be selected on basis of having
smoked less than 1 pack year and having no clinical signs of
emphysema. Lung cancer patients who undergo lobectomy /

pneumectomy will be selected on basis of the size and location of the tumor, enabling adequate collection of tissue material, without interfering with routine oncopathology procedures.

Exclusion criteria

Patients with alpha1antitrypsin deficiency will be excluded.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Control: N/A , unknown

Recruitment

NL

Recruitment status:	Other
Start date (anticipated):	01-03-2016
Enrollment:	20
Type:	Unknown

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL5523
NTR-old	NTR5664
Other	METc Universitair Medisch Centrum Groningen : 2015/599

Study results