Mesenchymal stem cells in emphysema: finding the right niche for alveolar repair

Published: 11-02-2016
Last updated: 20-04-2024

The projects is divided in 3 aims: 1) To evaluate the regenerative capacity of lung-derived MSCs (LMSCs) from normal and emphysematous lung tissue and compare LMCSs to MSCs derived from other tissues2) To investigate the interaction of MSCs with the...

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

Summary

ID

NL-OMON43398

Source
ToetsingOnline

Brief title
Mesenchymal stem cells in emphysema

Condition

- Respiratory disorders NEC

Synonym
emphysema and chronic bronchitis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: longfonds

Intervention

Keyword: COPD, emphysema, regenerative medicine, stem cells

Outcome measures

Primary outcome

•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.

Secondary outcome

n.v.t.

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 bio-active scaffolds. Recent studies indicate that especially the use of mesenchymal stem cells (MSCs) is promising. MSCs produce anti-inflammatory 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 lung-derived 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 bio-active scaffold potentially promotes MSC engraftment, tissue persistence and regenerative capacity, although knowledge on the optimal composition of such a scaffold is limited.

Study objective

The projects is divided in 3 aims:
1) To evaluate the regenerative capacity of lung-derived MSCs (LMSCs) from normal and emphysematous lung tissue and compare LMCSs to MSCs derived from other tissues
2) To investigate the interaction of MSCs with the micro-environment and construct bio-scaffolds that promote MSC function
3) To study the ability of in vitro-conditioned MSCs from emphysema patients to support alveolarization in vitro

Study design

This observational in-vitro study wants to compare tissue from emphysema and non-emphysema patients with respect to the 3 above described aims.

Study burden and risks

There are no benefits for participation in this study, nor risks or disadvantages. The potential value of the study is that at the long term new treatment options for severe emphysema patients will become available. The study needs to obtain tissue from emphysema and non-emphysema controls in order to characterize the insufficient regenerative capacity of mesenchymal cells from emphysema patients, and to optimize this until normal values.

Collection of lung resection material is not a safety issue from the perspective of this study. Lung resection is already performed in our patients for non-study reasons, as lung resection is part of routine treatment of very severe COPD (performing lung transplantation) or lung cancer (performing lobectomy/pneumectomy).

Collection of bronchial biopsies in severe emphysema is part of an ongoing research program in severe emphysema patients undergoing endobronchial lung volume reduction. This is safe and not a burden because the bronchoscopy takes place under general anesthesia and artificial ventilation. In addition, only very small biopsies are taken from central airway carina*s.

Collection of fat tissue is not part of routine treatment in these patients. But there is no extra burden for the patient as only 1cm3 of subcutaneous fat is harvested in the surgical incision. There is no significant bleeding risk and due to the low amount of sampled fat there are no cosmetic issues.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1 Hanzeplein 1
Groningen 9713 GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1 Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Lung resection material will be obtained from 6-10 COPD patients and 6-10 non-COPD 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. Patients with alpha-1 antitrypsin deficiency will be excluded. The non-COPD 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 LMSCs and extracellular matrix, without interfering routine oncopathology procedures.

Exclusion criteria

Patients with alpha-1 antitrypsin deficiency will be excluded.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-03-2016
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	11-02-2016
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	NL55903.042.15
Other	Tijdelijk kandidaat nr. 23712