Blood and Beyond: T-cell immunology in the human lungs

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Investigate the phenotype, function and regulation of TRM in healthy human lung tissue, lung tumors and peripheral blood to improve the understanding of respiratory diseases and adoptive T-cell therapy for lung cancer.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON42231

Source
ToetsingOnline

Brief title
Lung T-cells

Condition

- Other condition
- Respiratory tract neoplasms

Synonym
lung cancer

Health condition

general principles of respiratory tract disorders including infections and neoplasms

Research involving
Human

Sponsors and support

Primary sponsor: Sanquin Bloedbank
Source(s) of monetary or material Support: Landsteiner Foundation for Blood Transfusion Research (LSBR);Lung Foundation Netherlands

Intervention

Keyword: adaptive immune response, cancer, lung, T cell

Outcome measures

Primary outcome

Which regulatory circuits modulate T-cell phenotype and function in healthy

human lung tissue, lung tumors and peripheral blood

Secondary outcome

To answer the primary objective we want to perform the following analyses:

1) Optimization of the isolation of T-cells from tumor and lung tissue

(enzymatic digestion, collagenases, mechanical force).

2) Phenotypic comparison of T-cells derived from healthy lung tissue, lung

tumors and peripheral blood using multiparameter flow cytometry.

3) Investigation of the localisation of T-cells in healthy lung tissue and lung

tumors as well as their accessory cells using confocal microscopy.

4) Investigation of response of lung TRM and T-cells derived from tumor tissue

and peripheral blood to activating stimuli (antigen specific/non-specific

T-cell receptor stimulation, costimulation and cytokines) to analyse their

differential effector functions.

5) Comparison of the transcriptome and clonal composition (both genome wide and

T-cell receptor (TCR) sequence) of paired TRM, tumor and peripheral blood

derived T-cell populations.

6) Comparison of the proteome of paired TRM, tumor and peripheral blood derived

T-cell populations.

7) Combined analyses of the proteomes with the transcriptomes to reveal the

proteins that are regulated in a post-transcriptional manner.

Study description

Background summary

The lungs are the largest interphase between the body and the environment and are constantly engaged by inhaled pathogens. This makes the respiratory tract a prime site for the occurrence of infections and cancer and warrants the necessity of an active immunological defence. At the same time aberrant immune activation needs to be avoided to prevent collateral damage of the vital lung tissue. A delicate balance between protection and immunopathology needs to be maintained as dysregulation contributes to asthma, allergy and other lung diseases. Emerging evidence suggests that the recently described subset of resident memory T-cells (TRM), located in a variety of barrier tissues, mediates optimal protective immunity in the lungs. Little is known about how these cells are regulated, interact with other immunological subsets and contribute to inflammatory and autoimmune diseases.

Study objective

Investigate the phenotype, function and regulation of TRM in healthy human lung tissue, lung tumors and peripheral blood to improve the understanding of respiratory diseases and adoptive T-cell therapy for lung cancer.

Study design

This cross-sectional observational study involves an in-depth characterization of lung T-cell subsets and interacting immunological subsets. Gained insights will lead to further experimental investigation with the objective to study lung TRM regulation.

Study burden and risks

The participants of this study are, asked about their health history and smoking habits in case these are not already documented by the attending

physician upon admission. Additionally the participants undergo a one-time blood draw of 50ml from an existing intra-vascular catheter during the scheduled surgery. This does not cause any additional discomfort to the patient. The risks of this routine procedure are minimal and the withdrawal of such small volumes of blood is generally well tolerated. The participants do not benefit from the participation in this study. However, basic insights into immune responses in the healthy lungs and tumor microenvironment may lead to improved therapies against respiratory infections and lung tumors in the future.

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

In order to be eligible to participate in this study, a subject must meet all of the following

criteria:
- Adult (18+)
- Undergoing lobectomy or pneumectomy for an isolated primary lung tumor
- Undergoing lung tissue resection for a primary non-infectious pulmonary or pleural disease

Exclusion criteria

- Previous radiotherapy in which the lungs might have been directly in the radiation field
- Chemotherapy in the last 6 months
- Sleeve lobectomy, wedge resection or metastasectomy

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-02-2016
Enrollment:	250
Type:	Actual

Ethics review

Approved WMO Date:	23-07-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-11-2016

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL52453.100.15