STEM study - Specific Tissue Engineering in Medicine

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malabsorption conditions
Study type	Observational non invasive

Summary

ID

NL-OMON47644

Source
ToetsingOnline

Brief title
STEM study

Condition

- Malabsorption conditions
- Hepatic and hepatobiliary disorders
- Metabolism disorders NEC

Synonym
malabsorption disorders, metabolic diseases, various epithelial disorders

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,ZonMW-TAS;ZonMW-Vidi;Metakids

Intervention

Keyword: organoids, stemcells, tissue engineering, transplantation

Outcome measures

Primary outcome

Analyse developmental and functional properties of epithelial stem cells isolated from gastrointestinal tract or liver to elucidate the role of human gastrointestinal stem cells both in normal homeostasis and epithelial disorders.

Secondary outcome

Develop methods to generate intestinal tissue from both children and adults for transplantation purposes.

Study description

Background summary

The gastrointestinal mucosa has an amazing regenerative capacity, enabling rapid restoration of its physiological functions following injury. The ability to do this resides within the epithelial stem cells located in the bottom of the gastrointestinal epithelial units. Recent advances towards isolation and characterization of epithelial stem cells made it possible to explore therapeutic approaches based on tissue engineering for gastrointestinal epithelial diseases. Especially in cases of small intestinal and liver disease where standard treatment protocols (e.g. whole organ transplantation) are not sufficiently effective, there is a need for alternative therapeutic interventions, like adult stem cell transplantation.
Autologous tissue engineering is an attractive therapeutic alternative to organ transplantation. Recently, Hans Clevers et al have established a method that enables the growth of vast amounts of mouse intestinal and gastric tissue from intestinal crypts or gastric units. These 3-dimensional cultures have been shown to recapitulate in vitro the features of the in vivo epithelia, since they allow the maintenance of the stem cells and differentiated cells in culture in a so-called organoid or *mini-organ*. Furthermore, no genetic aberrations have been detected after months in culture, indicating that under

these culture conditions the cells are stable. Therefore, this culture system provides a unique opportunity to model the architecture of epithelium in vitro, facilitating the advance of tissue engineering.
Preliminary data show that it is feasible to generate organoids from human intestinal biopsies (T. Sato, personal communication). Another group of investigators communicated additional preliminary data in which they show that colonic organoids can be successfully transplanted into mice that have been treated with DSS to induce colitis. By using fluorescently-labeled organoids, they demonstrated proper engraftment of epithelial cells that were behaving similarly to endogenous tissue (T. Nakamura, personal communication).
These latest findings prompted us to pursue this technique to the next level and determine transplantation possibilities of engineered tissue from human gastrointestinal biopsies as an alternative treatment to whole organ transplantation. Furthermore, the in vitro system will be useful in studying pathogenesis of disease and develop and test novel treatment strategies (in a personalized setting).

Study objective

The STEM study presented here aims to increase our knowledge of the most common intestinal, gastric and liver epithelial diseases with the ultimate goal to treat these disorders.
Particularly, children that have severe malfunction of their gastrointestinal epithelium, like in cases of MVID, are completely dependent on TPN and are too young to undergo organ transplantation. For these patients, we aim to develop a transplantation method with engineered autologous tissue that is genetically modified to repair the original genetic defect or by using engineered tissue from close relatives.
In order to take this technique into the clinic, we need to enhance our knowledge about the differentiation of epithelial tissue in general and improve the techniques of tissue engineering. Therefore, we will take gastrointestinal epithelial biopsies or resected material into tissue engineering cultures in which we will determine the differentiation potential of the tissue-specific epithelial stem cells, the possibility to perform gene targeting on epithelial stem cells and the feasibility to use engineered tissue for transplantation purposes.

Study design

This is an observational study in which we will culture biopsy or resection material from epithelial tissue of both pediatric and adult patients in order to engineer epithelial tissue. The engineered tissue will be used to study the differentiation potency of tissue-specific stem cells. Furthermore, we will determine genomic status of the tissue and compare to healthy control to determine disease-related aberrancies. In case of rare diseases or unknown deficiencies, we will determine genetic abnormalities in DNA of patients.

The knowledge we obtain from this study will be used to set-up future intervention studies to transplant in vitro engineered specific tissue into patients with epithelial disorders. Furthermore, the method can be used as a modelsystem to study pathogenesis of disease and develop and test novel treatment strategies (in a personalized setting).

Study burden and risks

Despite the fact that every biopsy encompasses a certain risk (chance of performation during colonoscopy <1:1000), obtaining several additional biopsies will not significantly increase that risk. During the biopsy or surgical procedure, 4 additional biopsies per location or parts of the resected material will be processed for the STEM study and taken into culture. We will draw 10 ml of blood which will be used for DNA analysis. In future, we aim to engineer a vast amount of autologous tissue for transplantation purposes which may become a beneficial treatment for patients with similar diseases.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Patients that need to undergo biopsy or resection of gastrointestinal tract and/or liver. These include patients with suspected coeliakie, IBD, liver, oesophagus or stomach problems. We will include patients that undergo endoscopy for other reasons (like IBS or screening for cancer) as controls.

Exclusion criteria

Patients using anticoagulantia or patients with easily bleeding mucosa, like in haemophylia.

Study design

Design

Study type:	Observational non 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):	16-08-2011
Enrollment:	397
Type:	Actual

Ethics review

Approved WMO Date:	06-06-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-03-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	11-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-05-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-10-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-03-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-12-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL32324.041.10