Podocytes derived from induced pluripotent stem cells as biomarker of disease-causing mutations

Published: 19-08-2019
Last updated: 10-04-2024

1. To evaluate if podocytes directly cultured from the urine, and podocytes derived from induced pluripotent stem cells (iPSCs), can be used to prove causality of the VUS.2. Comparison of results obtained using iPSC-derived and urinary podocytes,...

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

Summary

ID

NL-OMON49859

Source
ToetsingOnline

Brief title
Podocytes from stem cells mimick disease

Condition

- Nephropathies

Synonym
collagen type IV nephropathy; hereditary nephritis

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Nierstichting Nederland

Intervention

Keyword: genetic diseases, podocyte, proteinuria

Outcome measures

Primary outcome

Abnormal function of podocytes from patients with proven disease causing

mutations compared to disease and healthy controls.

Secondary outcome

Not applicable

Study description

Background summary

Kidney diseases can be caused by mutations in genes that encode proteins involved in the functioning of epithelial cells of kidney filtering organs (podocytes) or the composition of the basement membranes. With increased use of DNA-sequencing, and the discovery of disease-causing mutations in the non-coding DNA (INTRONS), we now see many patients with a *genetic variant of unknown significance (VUS)*.

Study objective

1. To evaluate if podocytes directly cultured from the urine, and podocytes derived from induced pluripotent stem cells (iPSCs), can be used to prove causality of the VUS.
2. Comparison of results obtained using iPSC-derived and urinary podocytes, respectively.

Study design

1. Reprogramming of peripheral blood mononuclear cells (PBMC) obtained from patients and controls into induced pluripotent stem cells at the Radboudumc Stem Cell Technology Center (SCTC);
2. Induction of podocyte development from iPSCs, and culturing of podocytes from urinary cells at the Department of Pathology Research laboratory;
3. Evaluation of podocyte function (mRNA production, motility, protein

expression patterns).

Study burden and risks

Burden and risks associated with participation are minimal. A single visit to the outpatient clinic is required to obtain informed consent (IC) and perform one single venipuncture. We will draw 40 mL of heparanized blood for peripheral blood mononuclear cells (PBMC) reprogramming into iPSCs. We will also obtain a freshly voided urine for the purpose of podocyte culturing. No additional tests are required. Although the project is highly experimental, the benefit for patients will be potential development of a test that can be used to confirm disease-causality of a documented genetic variant. The risk benefit ratio is therefore very low.

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

1. Patients
* Established diagnosis of collagen IV nephropathy with disease-causing Col4 mutation.
2. Disease controls:
* diagnosis of focal segmental glomerulosclerosis (FSGS) with no evidence of underlying genetic mutations.
3. Healthy controls:
* no signs of kidney disease, negative family history of kidney diseases (i.e. proteinuria or hematuria with no proven cause).

Exclusion criteria

* Unspecified kidney injury;
* Not able to provide informed consent.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-10-2019
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	19-08-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-01-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL69788.091.19