GENETIC STUDIES OF CHRONIC KIDNEY DISEASE - GENEKID

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To elucidate the molecular mechanisms underlying renal disease that lead to chronic kidney disease. To validate pathogenic variations in functional in vivo models.

Ethical review	Approved WMO
Status	Pending
Health condition type	Renal and urinary tract disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON41287

Source
ToetsingOnline

Brief title
GENEKID

Condition

- Renal and urinary tract disorders congenital
- Autoimmune disorders
- Nephropathies

Synonym
Genetic Chronic Kidney Disease, glomerulonephritis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,National Institutes of Health (NIH);American Heart Association (AHA);American Society of Nephrology (ASN)

Intervention

Keyword: Chronic Kidney Disease, Genetics, International multicenter study, Whole-exome sequencing

Outcome measures

Primary outcome

Identification of rare known and novel variants (i.e. point mutations and

copy-number variations) underlying chronic kidney disease. These variants are

absent or extremely rare in the normal population.

Secondary outcome

By associating the genetic findings to the clinical data, we additionally aim

to establish genotype-phenotype correlation profiles for all investigated

phenotypes.

Study description

Background summary

Chronic kidney disease is a major public health problem resulting in significant morbidity and mortality. There is ample evidence for familial aggregation of chronic kidney disease, suggesting a genetic contribution. However, the genetic architecture of renal diseases is complex, with both structural variants as well as point mutations contributing to the variability in phenotypes. Moreover, mutations can have pleiotropic effects (i.e. the same mutation can lead to different phenotypes) and the inheritance of genetic renal traits follow a variable mode of inheritance (from X-linked to autosomal dominant). This complex make-up has hampered gene identification of these renal diseases until recently. Advancements in genotyping and sequencing methods as well as bio-informatics now allow discovery of disease-causing rare variants in (pediatric) renal disease such as congenital anomalies of the kidney and urinary tract (CAKUT), IgA nephropathy (IgAN), nephrotic syndrome and atypical hemolytic uremic syndrome (aHUS).

Study objective

To elucidate the molecular mechanisms underlying renal disease that lead to chronic kidney disease. To validate pathogenic variations in functional in vivo models.

Study design

Observational genetic studies by using state-of-the art high-throughput genetic techniques to identify genes implicated in genetic renal disease. In vivo animal models will be used to validate genetic findings (these studies will be performed at the coordinating center at Columbia University, New York, USA; patients will be recruited at the VU University Medical Center, Amsterdam, NL).

Study burden and risks

DNA will be obtained during the single routine, clinically indicated, venapunction at the outpatient clinic of the department of pediatric nephrology at the VU University Medical Center. As genetic renal diseases predominantly present during childhood, these studies will predominantly performed in minors. Because risks of participating are absent and no extra invasive procedures are necessary, the burden of participation in this study is negligible. Moreover, it is reasonable to expect that this study will increase our understanding of the pathophysiological mechanism of severe renal diseases, which imply major implications for the development of novel methods for diagnosis and treatment of subjects.

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

Subjects with genetic renal disease (congenital anomalies of the kidney and urinary tract, IgA-nefropathy (biopsy proven), nephrotic syndrome, atypical haemolytic uremic-syndrome (biopsy proven), cystinosis, renal tubulopathies) or children with a high susceptibility for genetic disease due to multiple extra-renal malformations (syndrome) or a positive family history
All ages

Exclusion criteria

Absence of informed consent
Pathogenic variant already known before study inclusion
Disapproval to be informed on genetic findings that are associated with hereditary diseases in later life (e.g. breast cancer, colon cancer, Huntington's disease)

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2015
Enrollment:	400
Type:	Anticipated

Ethics review

Approved WMO

Date:	02-04-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL43517.029.14