KDM2B and the epigenetic machinery: an iPSC-derived model of a novel neurodevelopmental syndrome

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neurological disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON51708

Source
ToetsingOnline

Brief title
KDM2B disorder

Condition

- Neurological disorders congenital

Synonym
KDM2B-associated syndrome, KDM2B-related disorder

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: WKZ fonds

Intervention

Keyword: genetics, iPSC, KDM2B, syndrome

Outcome measures

Primary outcome

This is a fundamental research study without clear defined end-points where we aim to develop an in vitro cell model of the KDM2B syndrome.

Secondary outcome

Inclusion of 15 patients and their clinical data entered in Castor, 6 skin biopsies, 5 successfully reprogrammed iPSC, 3 successful differentiation to neurons, 3 generated isogenic controls.

Study description

Background summary

Recently, we delineated a novel syndrome caused by heterozygous variants in the KDM2B gene (van Jaarsveld et al, submitted). Individuals present with developmental delay and/or intellectual disability, autism, ADHD and congenital organ anomalies. The role of KDM2B in human (neuro)development and the molecular mechanisms leading to this disorder remain to be elucidated. Affected individuals suffer lifelong from neurodevelopmental issues, and while there is potential reversibility by targeting epigenetic changes, there is a huge knowledge gap to be bridged rather sooner than later.

Study objective

Our main goal is to develop an in vitro model to investigate the function of wildtype and mutant KDM2B in neuronal development. We want to use this model to investigate genotype-phenotype correlations, elucidate isoform expression in neuronal development and study cellular and molecular effects of KDM2B variants. Furthermore, we want to determine clinical spectrum of KDM2B clinical disorder in more detail.

Study design

In this study, clinical data of individuals carrying KDM2B variants is collected (retrospective cohort study). Next to this aspect, this study consists of fundamental research, as patient fibroblasts are collected and used to develop an in vitro model to investigate the consequences of mutant KDM2B on neuronal development.

Study burden and risks

The burden can be considered low since the study participation only consists of one hospital visit and (optional) one punch skin biopsy under local anesthesia. This procedure can leave a 3-4mm scar on the arm. This biopsy is generally considered a safe procedure, and rare complications of skin biopsy are relatively mild (infection, prolonged bleeding and/or hematoma of the biopsy site).
This study could not be conducted without the participation of subjects belonging to the group in question. This study is essential for further research into their disorder, which is not performed elsewhere. In this way, the outcomes can be potentially important for the subjects as well as it will provide novel insights on the etiology of this disorder.

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

a variant in the KDM2B gene
OR having a child with a KDM2B variant who has been included in the study for skin biopsy

Exclusion criteria

If the subject or legal caretakers are unable to provide consent
Severe bleeding disorder expected to lead to a complicated skin biopsy
Known allergy to all available local anaesthetics

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:	Recruiting
Start date (anticipated):	30-01-2023

Enrollment:	26
Type:	Actual

Ethics review

Approved WMO Date:	08-11-2022
Application type:	First submission
Review commission:	METC NedMec

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	NL81759.041.22