Discordant Monozygotic Twinning in Beckwith-Wiedemann Syndrome: A Study of Embryonic Pluripotency and Epigenetic Reprogramming

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Investigating the molecular and phenotypic differences of iPSCs established from skin fibroblasts of discordant MZ BWS twin pairs.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational invasive

Summary

ID

NL-OMON44262

Source
ToetsingOnline

Brief title
Discordant MZ Twins with BWS

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
Beckwith-Wiedemann Syndrome; BWS

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Beckwith- Wiedemann Syndrome, epigenetics, iPSC, monozygotic

Outcome measures

Primary outcome

The molecular and phenotypic differences of naïve and primed iPSCs obtained

from discordant BWS MZ twins.

Secondary outcome

Obtaining insight in the mechanism behind the splitting of the ICM for the

birth of identical twins, which will have direct relevance to the study of

embryonic pluripotency.

Study description

Background summary

Beckwith-Wiedemann Syndrome (BWS) is an overgrowth congenital disorder with an increased frequency of monozygotic (MZ) twinning, in which the MZ twins predominantly are discordant for BWS. The aetiology of this increased MZ twinning frequency remains unknown. Examining this unique phenomenon is expected lead to a better understanding of the process of MZ twinning, epigenetic methylation disturbances, and human embryonic pluripotency. We hypothesize that by investigating the molecular and phenotypic differences of induced pluripotent stem cells (iPSCs) derived from skin fibroblasts of discordant BWS MZ twin pairs the pathogenesis of this process can be uncovered.

Study objective

Investigating the molecular and phenotypic differences of iPSCs established from skin fibroblasts of discordant MZ BWS twin pairs.

Study design

Case-control study in which within each MZ twin pair the healthy twin controls for the BWS twin.
In participants 16 years or above a skin biopsy will be performed; in

participants under 16 years of age subcutis will be obtained during a surgical intervention performed for care purposes.

Study burden and risks

A skin biopsy in an adult causes limited burden to a person. A biopsy of 2-3 mm does not need stitching, and leaves a very small scar. Obtaining subcutis from an incision during surgery in a child causes no burden to the child. There is no benefit for the participants. In the future there may be a group benefit if it offers insight in the occurrence of methylation disturbances that can be prevented.

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

1) Monozygotic twins
2) Discordant for Beckwith-Wiedemann syndrome
3) BWS clinical diagnosis molecularly confirmed
4) Able and willing to provide written informed consent to the study

Exclusion criteria

none

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-02-2018
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	01-09-2017
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	NL62045.018.17