TwinLife: TWIN Longitudinal Investigation of FEtal discordance

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON22667

Source
NTR

Brief title
TwinLife

Health condition

Monochorionic twin pregnancies

Sponsors and support

Primary sponsor: The Dutch Heart Foundation
Source(s) of monetary or material Support: The Dutch Heart Foundation

Intervention

Outcome measures

Primary outcome

1. Percentage difference in DNA methylation in MSCs at birth within MC twin pairs in relation to measures of intra-uterine discordance: percentage difference in birthweight and percentage difference in placenta share.
2. Within-twin pair differences at follow-up in childhood (2, 5, 8 years) with respect to risk of CVD and NDI as explained by the DNA methylation differences at birth. Study parameters of

CVD at follow-up: cardiac load reflected by left-ventricular mass, vascular stiffness reflected by aortic pulse-wave velocity

Secondary outcome

1. Explore the persistence of epigenetic differences in peripheral tissues (buccal swabs) from birth to 2, 5 and 8 years follow-up.
2. Test the association of epigenetic changes in MSC cells with cellular metabolism.
3. Correlate within-pair differences in fetal cardiac growth and function and outcome at birth and at follow-up.

Study description

Background summary

Lifelong health is in part set during intrauterine life. An adverse intrauterine environment can induce persistent epigenetic changes that are thought to cause long-term health effects. There is an urgent need for human studies that can identify the epigenetic alterations that underlie the impact of intrauterine adversity on disease, in particular cardiovascular disease (CVD) and neurodevelopmental impairment (NDI). This study will focus on identical twin pairs who shared a single placenta i.e., monochorionic (MC) twins. Every year, over 600 MC twins are born in The Netherlands and they are at high risk of experiencing an adverse intrauterine environment. In one third of pairs, one fetus has significantly less access to nutrients and resources during pregnancy than its co-twin, conditions known to be linked to increased CVD risk and impaired neurodevelopment in adults. Thus, although genetically identical, great differences in intrauterine exposure exist within twin pairs, providing an unique natural experiment allowing a robust assessment of the development of cardiac- and neurodevelopmental risk factors in childhood and probe the underlying epigenetic mechanisms. Instead of relying on commonly used blood samples, this study will examine altered epigenetic regulation in mesenchymal stromal cells (MSCs), an enhanced proxy for other tissues involved in CVD and NDI. These multipotent cells are known to display metabolic changes in newborns exposed to an adverse intrauterine environment and can be differentiated into other cell types. The hypothesis is that twins discordant for pregnancy complications display a distinct epigenetic signature in MSCs. This signature contributes to cellular metabolic alterations and is associated with future cardiovascular and neurodevelopmental outcome in childhood and beyond. Our results will not only address an unmet clinical need in the high-risk group of MC twins, but may also advance early-life CVD prevention strategies and underpin their efficacy in the general population.

Study objective

The hypothesis is that twins discordant for pregnancy complications display a distinct epigenetic signature in MSCs. This signature contributes to cellular metabolic alterations and is associated with future cardiovascular and neurodevelopmental outcome in childhood and

beyond.

Study design

Prenatal; birth; 6 months; follow-up at 2, 5 and 8 years

Contacts

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Eligibility criteria

Inclusion criteria

- MC twin pregnancies
- Parents aged ≥ 18 years, who are able to consent
- Written informed consent from both parents to participate in this longitudinal study

Exclusion criteria

- The presence of major anatomical abnormalities
- Triplet pregnancies or higher order multiple pregnancies
- Twin reversed arterial perfusion (TRAP)
- MC twins with single or double fetal demise

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-01-2019
Enrollment:	200
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	22-02-2019
Application type:	First submission

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
NTR-new	NL7538
Other	METC LUMC : P18.184

Study results