Circulating cell free DNA: the fingerprint of the Placenta

Published: 30-05-2024
Last updated: 07-12-2024

Identifying placental disease during pregnancy using cfDNA of placental cells in the maternal circulation to discover new therapeutic placental targets for fetal treatment.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Placental, amniotic and cavity disorders (excl haemorrhages)
Study type	Observational invasive

Summary

ID

NL-OMON56768

Source
ToetsingOnline

Brief title
FIERCE

Condition

- Placental, amniotic and cavity disorders (excl haemorrhages)

Synonym
Placental disease

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Cell free DNA, DNA methylation, Inflammation, Placenta

Outcome measures

Primary outcome

To determine the methylation profiles of placental cell populations of:

- uncomplicated pregnancies (controls).

- inflammation in the placenta (cases).

Secondary outcome

- Identify underlying genes or genetic pathways related to identified

methylation placental profiles of involved in (ab)normal placental development.

- Define placental markers that can predict an abnormal inflamed placenta

(chorioamnionitis and intervillositis).

Study description

Background summary

So far, it is only possible to assess placental abnormalities after birth with histological analysis. To treat placental abnormalities during pregnancy, it is important to recognize placental abnormalities as early as possible, before birth. The 2 most common inflammatory placental abnormalities that cause poor pregnancy outcomes are chorioamnionitis and intervillositis. Fragments of the placenta are known to be present in the mother's blood (cfDNA). With a new technique; Methylation sequencing (MeD-seq) we are going to identify for the first time the DNA profiles of these placenta fragments in the mother's blood (cfDNA). With this pilot study, we aim to investigate the most common inflammatory placental abnormalities that cause poor pregnancy outcomes such as fetal distress, asphyxia and (intra uterine) death. This will be the first prenatal test to recognize inflammatory placental damage. This will allow us in the future to assess the placenta earlier, during pregnancy without harming the baby.

Study objective

Identifying placental disease during pregnancy using cfDNA of placental cells in the maternal circulation to discover new therapeutic placental targets for

fetal treatment.

Study design

A single center prospective observational pilot cohort study will be at one timepoint at delivery of the baby/placenta at the Erasmus MC.

Study burden and risks

No experimental medication will be used. Women will be treated according to local hospital protocol. No additional risks or burden are expected from the study.

Risks for obtaining maternal blood: For all 30 cases, the risks involve primarily the burden of participating in a study. For this study we need 20 ml blood which will be collected during the regular venapunction in the hours before labour needed for clinical parameters. There will be no extra hospital visit or no extra time point of the venapunction. Participants will not undergo any additional procedures. However, the blooddrawing will take extra time as 4 vials (total 20 ml) will be needed for this study. The risks of participation are considered to be very low.

Risks for placental sample: No site visits, no participation of patients required. No treatment. The placentas of the patients are always stored for clinical analysis. If patients are willing to give consent this tissue can be used for future research. We use material from the pathology archive that can be used for research. There is an opt-out regulation with a database. For every sample the pathology department checks if the patient has given permission for using their tissue for research.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

General:
- Pregnant women >= 18 years and <= 45 years who are willing to participate.
- Sufficient understanding of Dutch in speaking and reading.
- Willingness to give written informed consent.
- Singleton pregnancy.
- Blood drawing (venapunction) planned for clinical purposes.

Two patient groups are eligible:
- Healthy pregnant women with an uncomplicated pregnancy (10 controls).
- Healthy pregnant women with a premature delivery (between 24 and <37 weeks) clinically with suspicion of inflammation (20 cases).

Placentas from the pathology archive that can be used for research for a baseline quality check:
- 10 placentas from an uncomplicated pregnancy (controls)
- 10 placentas with a premature delivery (between 24 and <37 weeks) clinically with suspicion of inflammation (cases)

Exclusion criteria

Multiple pregnancy.
- Gastro-intestinal diseases, heart diseases, liver, pancreas and kidney diseases.
- Pre-existent diabetes mellitus.
- Unable or unwilling to give informed consent.
- Fetus with a known congenital/chromosomal abnormality.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-07-2024
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	30-05-2024
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL86223.078.24