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Measuring levels of maternal cell microRNAs to predict adverse pregnancy outcome

Submission date 25/12/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 09/01/2018	**Overall study status** Completed	
Last Edited 01/07/2021	**Condition category** Pregnancy and Childbirth	

Plain English summary of protocol

Background and study aims
The aim of this study is to develop a first trimester predictor test for identifying pregnant women at high risks of various pregnancy complications. These complications include high blood pressure in pregnancy (known as pre-eclampsia), miscarriage (pregnancy loss) and spontaneous pre-term birth (premature delivery from 24 to 36 weeks of pregnancy). This predictor test will measure the levels of specific microRNAs from a blood test. microRNAs are small molecules which contain genetic material that is essential for all known forms of life. They control gene expression and regulate many proteins. High levels of miRNAs have been shown to decrease certain gene expression pathways believed to play a role in the development of a healthy pregnancy. This study may help to identify pregnant women who are at high risk of developing pregnancy complications. The outcome of this study may alter the management of future pregnant women deemed to be at risk of developing these adverse outcomes.

Who can participate?
Pregnant women aged 24 to 43

What does the study involve?
Participants provide blood samples at 8-10 weeks of pregnancy. Also, if the participant chooses to return for NIPT (non-invasive prenatal testing) where a blood test is routinely drawn, a very small volume of blood is also drawn for the purpose of this study. The levels of specific miRNAs are measured. Participants are asked to fill out a questionnaire detailing their pregnancy after 9 months. The history of the pregnancy is then compared to the level of miRNAs in the blood.

What are the possible benefits and risks of participating?
There are no direct benefits to those participating. However, the information obtained from this study may help to identify patients who are at high risks of pre-eclampsia, miscarriage or spontaneous preterm delivery. This may result in a change in the management of pregnant women who are identified at risk of adverse pregnancy, and minimise the risk of complications. Drawing blood for normal screening does not carry any risks and participating in this study is not expected to add any further risks.

Where is the study run from?
The Centre for Reproductive and Genetic Health (UK)

When is the study starting and how long is it expected to run for?
December 2017 to August 2025

Who is funding the study?
The Centre for Reproductive and Genetic Health (UK)

Who is the main contact?
1. Ms Jara Ben-Nagi (scientific)
2. Miss Rabi Odia (public)

Contact information

Type(s)
Scientific

Contact name
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Type(s)
Public

Contact name
Miss Rabi Odia

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
miRNA

Study information

Scientific Title
Measuring levels of maternal cell microRNAs to predict adverse pregnancy outcome: a longitudinal observational study

Study objectives
Can levels of maternal microRNAs become a first trimester “predictor” test for identifying high risk of an adverse pregnancy outcome (including pre-eclampsia, miscarriage, etc)?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Single-centre longitudinal observational study

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Other

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Couples that have successfully conceived

Interventions
Peripheral blood is drawn from a pregnant patient at 8-10 weeks, the sample undergoes separation/extraction of PBMCs which is stored at -80°C. miRNA isolation, miRNA quantification, reverse transcription, and real-time PCR will be carried out. Patients who have participated in this study are then asked to fill out a questionnaire detailing their pregnancy after 9 months. The history of pregnancy will then be compared to the level of microRNA in peripheral blood.

1. Sample collection: After obtaining patient consent. Peripheral blood from successfully conceived patients at 8-10 weeks will be collected in Heparin tubes (green top) and incubated at room temperature for 1-2 hours
2. Separation of PBMCs from peripheral blood and storage: Separation/extraction of PBMCs will be performed at room temperature using Ficollhypaque density gradient centrifugation. The

PBMCs layer will be “pipetted” into tubes containing 1ml of Trizol and stored at -80oC
3. Molecular techniques: miRNA isolation, miRNA quantification, reverse transcription, and real-time PCR will be performed by igenomix UK
4. Analysis, statistics and reporting: Will be performed by Igenomix UK scientific staff
5. Follow up: Collection of patient birth and adverse outcomes will be conducted by CRGH. Once the agreed endpoint is reached, the sample IDs will be unblinded and the results shared between CRGH and Igenomix UK in preparation for publication

Intervention Type
Other

Primary outcome measure
Levels of specific miRNAs isolated from maternal peripheral blood mononuclear cells (PBMCs) in 8-10-week pregnant patients, measured by real-time PCR using TaqMan probes after reverse transcription

Secondary outcome measures
Pregnancy outcome assessed using a questionnaire after 9 months

Overall study start date
04/12/2017

Completion date
01/08/2025

Eligibility

Key inclusion criteria
Successfully pregnant healthy females aged between 24 and 43

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
24 Years

Upper age limit
43 Years

Sex
Female

Target number of participants
209

Key exclusion criteria
Under 24 and over 43 years old females who are pregnant

Date of first enrolment
30/01/2018

Date of final enrolment
30/09/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Centre for Reproductive and Genetic Health
230-232 Great Portland Street
London
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Sponsor information

Organisation
Centre for Reproductive and Genetic Health

Sponsor details
230-232 Great Portland Street
London
England
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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Hospital/treatment centre

Funder Name

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal

Intention to publish date
01/08/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the Centre for Reproductive and Genetics Health (jarabennagi@crgh.co.uk). Data will be available upon completion of the study for a minimum of 5 years. Data will be accessed via an internal shared drive. Access to the shared drive has a designated username and password. The access will only be to the designated research members via an NHS secure web if receiving party also has access to this and password protected. This will be shared with iGenomix UK and only be available upon request. Consent will be obtained from the patients. The data will only contain participants' internal reg number and is password protected.

IPD sharing plan summary
Available on request