

Evaluation of levels of circulating mitochondrial DNA in maternal blood as markers of Intrauterine Growth Disorders

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BACKGROUND

- Intrauterine growth disorders also known as fetal growth disorders is the inability of a fetus to reach its capacity for growth.
- Cell free DNA from the fetus and the placenta releases into the maternal bloodstream.
- The shedding of fetal and placental DNA into maternal circulation may be altered in pregnancies with intrauterine growth disorders.
- The total circulating nucleic acids isolated from maternal plasma can be quantified using marker-specific assays.
- By targeting the KRAS (nuclear) and MT-COX3 (mitochondrial) genes, a mitochondrial to nuclear DNA ratio (MNR) could be a useful marker for fetal growth disorders.
- The mitochondrial-to-nuclear ratio (MNR) will equal the ratio of the concentration of the Mitochondrial cell free DNA (McfDNA) to Nuclear cell free DNA (NcfDNA), calculated through short base pair sequence amplification.
- Long and short fragments of nuclear and mitochondrial DNA will be quantified to evaluate DNA fragmentation by calculating the DNA integrity index (DII), expressed as the ratio between long and short sequence concentrations.
- The lower the DII, the more cfDNA is fragmented.

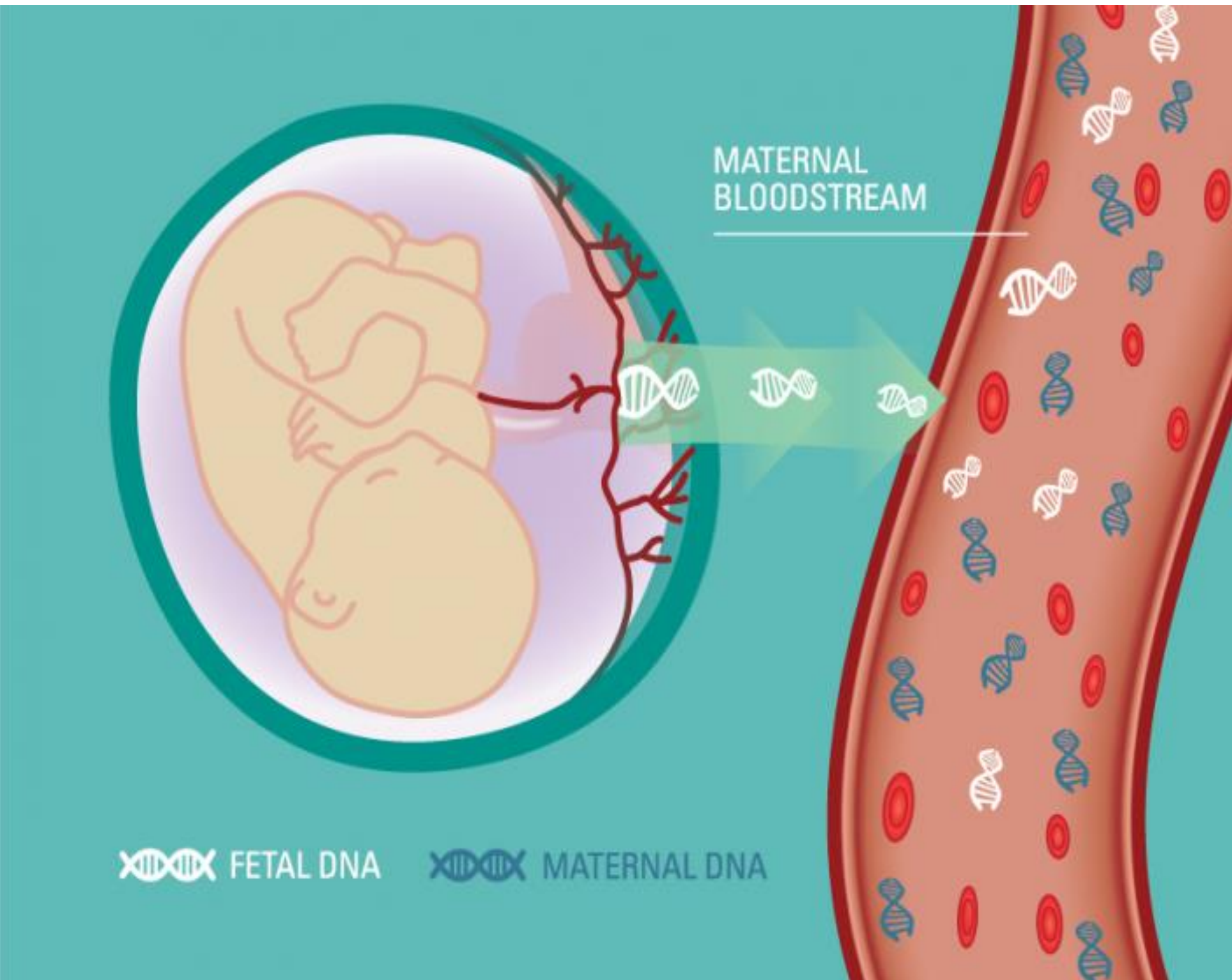


Figure 1: Fetal DNA is released through the placenta into the bloodstream of the mother.
Image: http://www.nipt.se/wp-content/uploads/2016/10/fetus_bloodstream-1.png

Hypothesis:

The Mitochondrial/Nuclear DNA ratio can serve as a marker for fetal growth disorders.

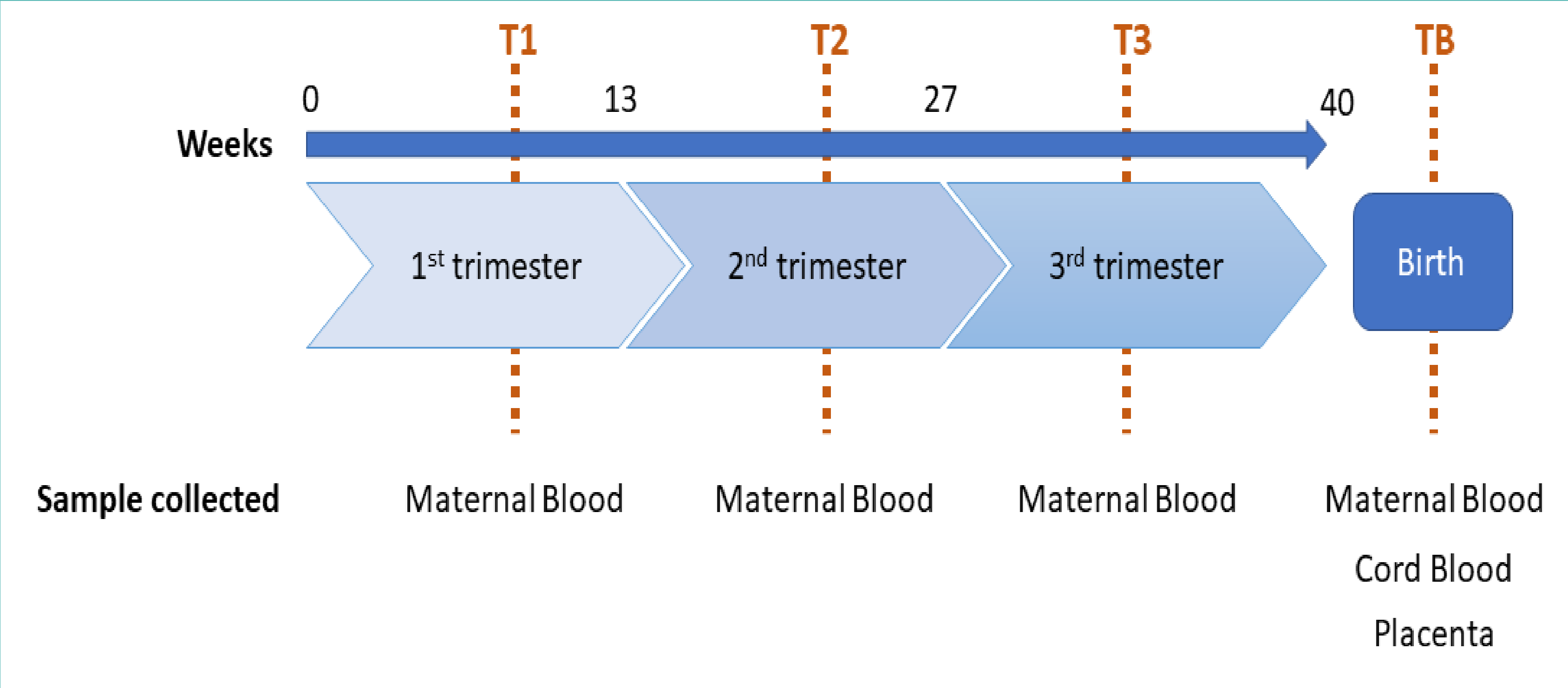


Figure 2: Blood sample time points

METHODS

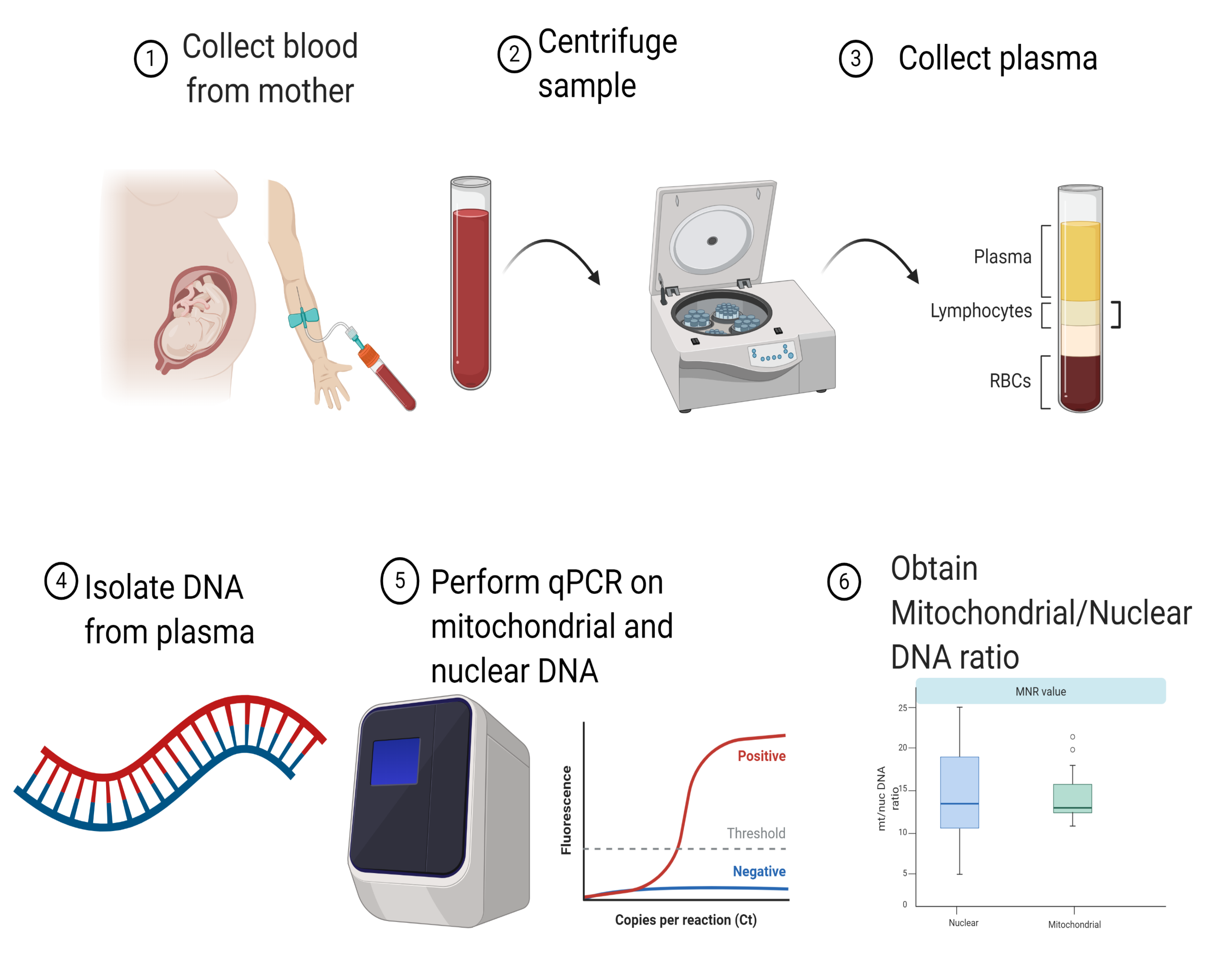


Figure 3: Flowchart of DNA isolation and qPCR

ANTICIPATED RESULTS

- Samples collected in each trimester will be compared per patient.
- Concentrations will be expressed in ng/mL.
- The MNR value will indicate the ratio of the mitochondrial and nuclear cfDNA present in the maternal plasma.
- We anticipate that the MNR might be significantly different in pregnancies with Intrauterine Growth Disorders compared with normal growing pregnancies.

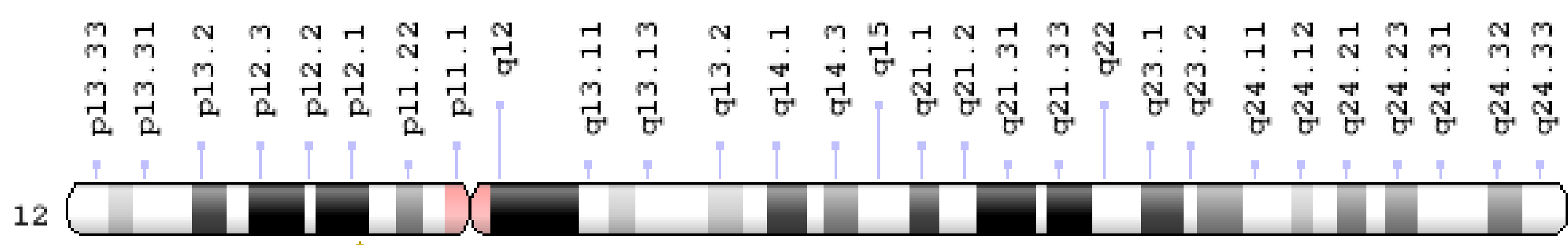


Figure 4: KRAS gene locus on chromosome 12.
Image: Genome Decoration Page/NCBI

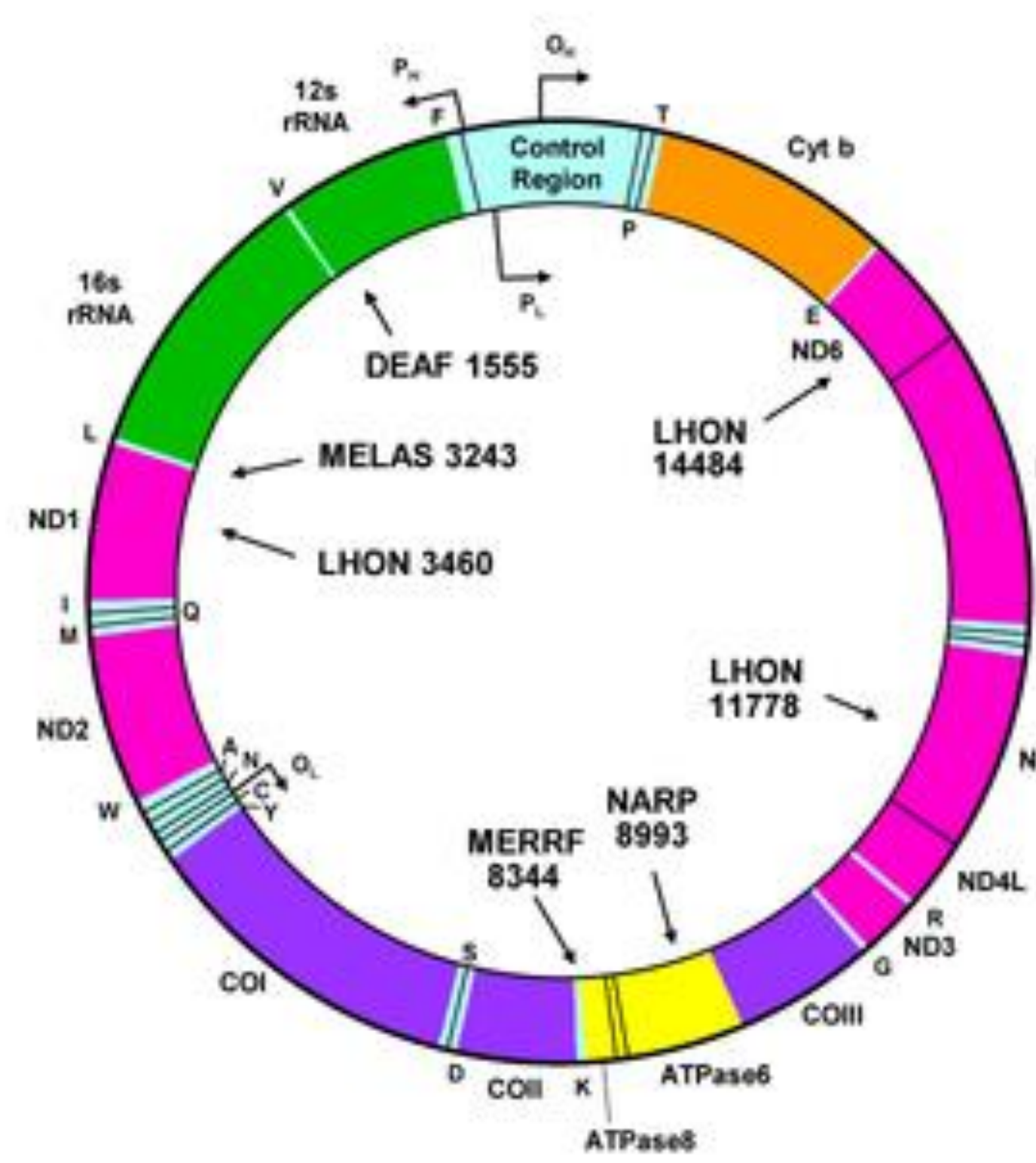


Figure 5: MT-COX3 gene locus on mitochondria. Image: MITOMAP: A Human Mitochondrial Genome Database. <http://www.mitomap.org>, 2019

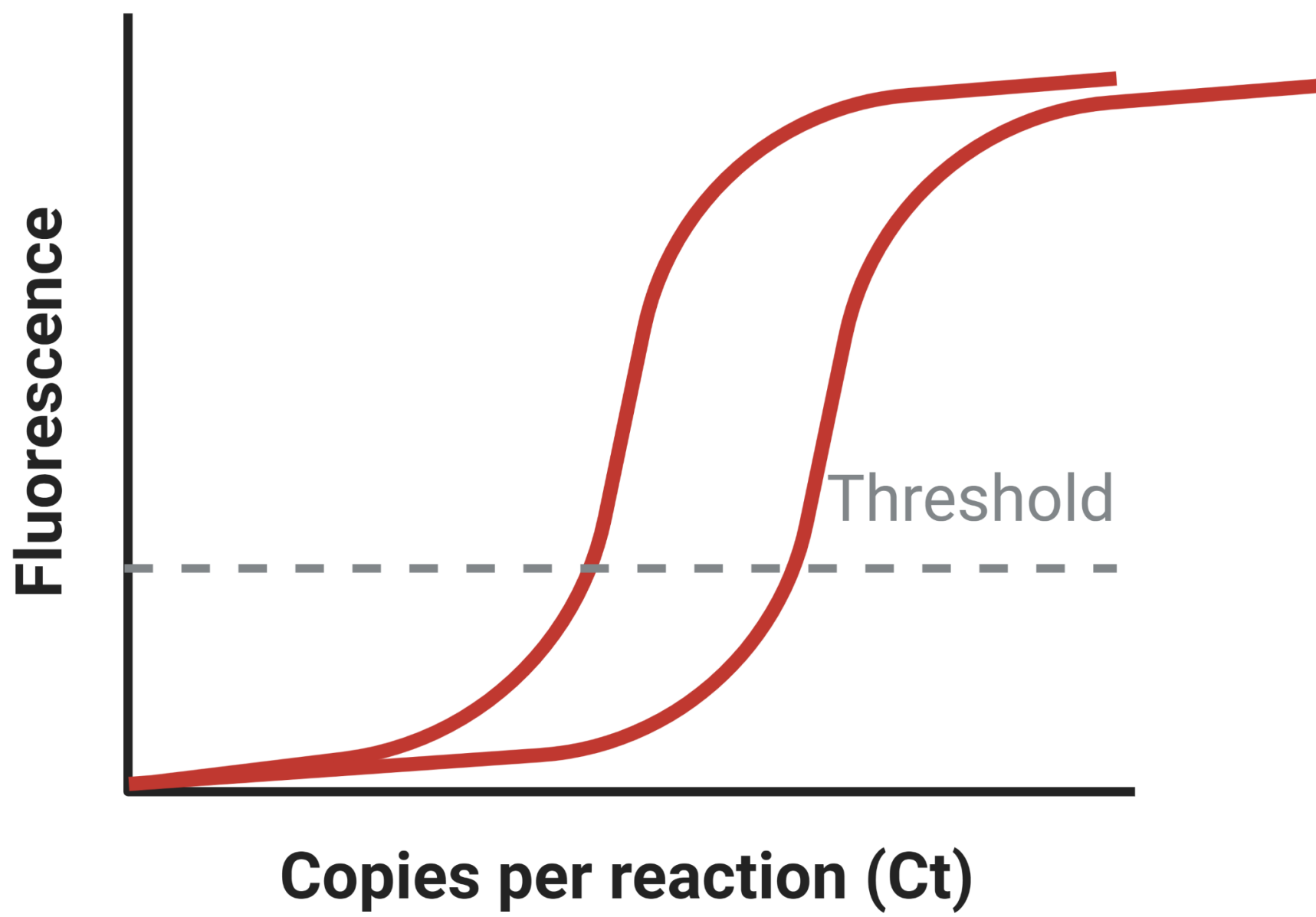


Figure 6: Real time PCR results graph

ANTICIPATED SIGNIFICANCE

- We anticipate that the MNR may be associated with the presence of fetal growth disorders and may hold potential as low-invasiveness prenatal biomarker
- These disorders will be predicted and identified sooner, and physicians will be able to create plans can be created for each patient to treat them according to their individual disorders.