

WHAT IS CLAIMED IS:

1. A non-invasive prenatal testing method comprising the steps of:

1) producing total nucleotide sequence fragments from cell-free DNAs extracted from maternal blood;

2) arranging the total nucleotide sequence fragments produced in step 1) at homologous positions of a human reference genome sequence;

3) dividing the total nucleotide sequence fragments arranged in step 2) into fetal nucleotide sequence fragments and maternal nucleotide sequence fragments according to a length, and calculating z-scores for the total nucleotide sequence fragments, the fetal nucleotide sequence fragments, and the maternal nucleotide sequence fragments, respectively; and

4) determining maternal mosaicism or fetal aneuploidy by comparing the z-scores for the total nucleotide sequence fragments, the fetal nucleotide sequence fragments, and the maternal nucleotide sequence fragments which are calculated in step 3).

wherein in the process of dividing the total nucleotide sequence fragments into the fetal nucleotide sequence fragments and the maternal nucleotide sequence fragments according to a length, the fetal nucleotide sequence fragments are isolated by 150 bp or less and the maternal nucleotide sequence fragments are isolated by 185 bp or more,

wherein the z-scores are calculated by the following Equation 1:

[Equation 1]

$$Z\text{-score}_{(chromosome\ i)} = \frac{Normalized\ Value_{(target\ i)} - Mean_{(reference\ i)}}{Standard\ Deviation_{(reference\ i)}}$$

wherein i refers to chromosomes 1 to 22, and an X chromosome or Y chromosome, reference refers to a normal sample group, and target means a maternal sample to be tested.

2. The non-invasive prenatal testing method of claim 1, wherein the nucleotide sequence fragments are produced by a massively parallel signature sequencing method.

3. The non-invasive prenatal testing method of claim 1, wherein the maternal mosaicism or fetal aneuploidy is determined as follows:

i) if the z-score for the fetal nucleotide sequence fragment is greater than the z-score for the total nucleotide sequence fragment, it is determined that the fetus is trisomy;

ii) if the z-score for the maternal nucleotide sequence fragment is greater than the z-score for the total nucleotide sequence fragment, it is determined as maternal mosaicism;

iii) if the z-score for the fetal nucleotide sequence fragment is smaller than the z-score for the total nucleotide sequence fragment, it is determined that the fetus is monosomy; or

iv) if the z-score for the maternal nucleotide sequence fragment is smaller than the z-score for the total nucleotide sequence fragment, it is determined as maternal mosaicism.

4. The non-invasive prenatal testing method of claim 1, wherein the fetal aneuploidy is determined as follows:

i) if the z-score for the fetal nucleotide sequence fragment is greater than the z-score for the total nucleotide sequence fragment, and

ii) if the z-score for the maternal nucleotide sequence fragment is smaller than the z-score for the total nucleotide sequence fragment, it is determined that the fetus is trisomy.

5. The non-invasive prenatal testing method of claim 1, wherein the fetal aneuploidy is determined as follows:

i) if the z-score for the fetal nucleotide sequence fragment is smaller than the z-score for the total nucleotide sequence fragment, and

ii) if the z-score for the maternal nucleotide sequence fragment is greater than the z-score for the total nucleotide sequence fragment, it is determined that the fetus is monosomy.

6. The non-invasive prenatal testing method of claim 1, wherein autosomal abnormality, sex chromosomal abnormality, or autosomal deletion is determined.

7. The non-invasive prenatal testing method of claim 6, wherein the autosomal abnormality causes Down syndrome, Edward syndrome, Patau syndrome, trisomy 9, trisomy 16, or trisomy 22.

8. The non-invasive prenatal testing method of claim 6, wherein the sex chromosomal abnormality causes Turner syndrome, Triple X syndrome, Klinefelter syndrome or Jacobs syndrome.

9. The non-invasive prenatal testing method of claim 6, wherein the autosomal deletion causes 1p36 deletion syndrome, 2q33.1 deletion syndrome, Wolf-Hirschhorn syndrome, cat crying syndrome, Williams syndrome, Jacobson syndrome, Prader-Willi/Angelman syndrome or DiGeorge syndrome.

10. A non-invasive prenatal testing apparatus comprising:

1) a production unit configured to produce total nucleotide sequence fragments from cell-free DNA extracted from maternal blood;

2) an arrangement unit configured to arrange the total nucleotide sequence fragments produced in step 1) at homologous positions of a human reference genome sequence;

3) a calculation unit configured to divide the total nucleotide sequence fragments arranged in step 2) into fetal nucleotide sequence fragments and maternal nucleotide sequence fragments according to a length and calculate z-scores for the total nucleotide sequence fragments, the fetal nucleotide sequence fragments, and the maternal nucleotide sequence fragments, respectively; and

4) a determination unit configured to determine maternal mosaicism or fetal aneuploidy by comparing the z-scores for the total nucleotide sequence fragments, the fetal nucleotide sequence fragments, and the maternal nucleotide sequence fragments which are calculated in step 3),

wherein in the process of dividing the total nucleotide sequence fragments into the fetal nucleotide sequence fragments and the maternal nucleotide sequence fragments according to a length, the fetal nucleotide sequence fragments are isolated by 150 bp or less and the maternal nucleotide sequence fragments are isolated by 185 bp or more,

wherein the z-scores are calculated by the following Equation 1:

[Equation 1]

$$Z-score_{(chromosome\ i)} = \frac{Normalized\ Value_{(target\ i)} - Mean_{(reference\ i)}}{Standard\ Deviation_{(reference\ i)}}$$

wherein i refers to chromosomes 1 to 22, and an X chromosome or Y chromosome, reference refers to a normal sample group, and target means a maternal sample to be tested.