Annex

1. A method for performing prenatal diagnosis of a fetal chromosomal aneuploidy in a biological sample obtained from a pregnant female subject, wherein the biological sample is maternal plasma and includes nucleic acid molecules, the method comprising:

receiving the biological sample;

randomly sequencing at least a portion of a plurality of the nucleic acid molecules contained in the biological sample, wherein the sequenced portion represents a fraction of the human genome;

based on the sequencing:

determining a first amount of a first chromosome from sequences identified as originating from the first chromosome;

determining a second amount of one or more second chromosomes from sequences identified as originating from one of the second chromosomes;

determining a parameter from the first amount and the second amount;

comparing the parameter to one or more cutoff values; and

based on the comparison, determining a classification of whether a fetal chromosomal aneuploidy exists for the first chromosome.

2. The method of claim 1, wherein the first chromosome is chromosome 21, chromosome 18, chromosome 13, chromosome X, or chromosome Y.

3. The method of claim 1, wherein the parameter is a ratio of sequences that originate from the first chromosome.

4. The method of claim 3, wherein the ratio is obtained from any one or more of a fractional count of the number of sequenced tags, a fractional number of sequenced nucleotides, and a fractional length of accumulated sequences.

5. The method of claim 3, wherein the sequences that originate from the first chromosome are selected to be less than a specified number of base pairs.

6. The method of claim 5, wherein the specified number of base pairs is 300bp, 200bp, or 100bp.

7. The method of claim 1, wherein the nucleic acid molecules of the biological sample have been enriched for sequences originating from at least one particular chromosome.

8. The method of claim 1, wherein the nucleic acid molecules of the biological sample have been enriched for sequences less than 300 bp.

9. The method of claim 1, wherein the nucleic acid molecules of the biological sample have been enriched for sequences less than 200 bp.

10. The method of claim 1, wherein the nucleic acid molecules of the biological sample have been amplified using a polymerase chain reaction.

11. The method of claim 1, wherein the fraction represents at least 0.1% or at least 0.5% of the human genome.

12. The method of claim 1, wherein a cutoff value is a reference value established in a normal biological sample.

13. The method of any preceding claim wherein the nucleic acid molecules are amplified by emulsion PCR.

14. The method of any preceding claim wherein the nucleic acid molecules are DNA.

15. The method of any preceding claim wherein the fractional concentration of fetal DNA in the maternal plasma is measured and the fractional concentration of fetal DNA is used to calculate the one or more cutoff values.

16. The method of any preceding claim wherein performing a random sequencing comprises sequencing the full length of short nucleic acid fragments to determine their length.

17. The method of claim 16 further comprising focusing the data analysis on the subset of sequences corresponding to short nucleic fragments in the biological sample by post-sequencing *in silico* selection.

18~~13~~. A computer program product comprising a computer readable medium encoded with a plurality of instructions for controlling a computing system to perform an operation for performing prenatal diagnosis of a fetal chromosomal aneuploidy in a biological sample obtained from a pregnant female subject, wherein the biological sample is maternal plasma and includes nucleic acid molecules, the operation comprising the steps of:

receiving data from a random sequencing of a portion of the nucleic acid molecules contained in the biological sample obtained from a pregnant female subject, wherein the biological sample includes nucleic acid molecules, wherein the portion represents a fraction of the human genome;

based on the data from the random sequencing:

determining a first amount of a first chromosome from sequences identified as originating from the first chromosome;

determining a second amount of one or more second chromosomes from sequences identified as originating from one of the second chromosomes;

determining a parameter from the first amount and the second amount;

comparing the parameter to one or more cutoff values; and

based on the comparison, determining a classification of whether a fetal chromosomal aneuploidy exists for the first chromosome.

19. The computer program product of claim 18 wherein the random sequencing uses emulsion PCR.

20. The computer program product of claim 18 or 19 wherein the nucleic acid molecules are DNA.

21. The computer program product of claims 18 to 20 wherein the operation further comprises the steps of measuring the fractional concentration of fetal DNA in the maternal plasma and using the fractional concentration of fetal DNA to calculate the one or more cutoff values.

22. The computer program product of claims 18 to 21 wherein the random sequencing comprises sequencing the full length of short nucleic acid fragments to determine their length.

23. The computer program product of claim 22 wherein the operation further comprises the step of focusing the data analysis on the subset of sequences corresponding to short nucleic fragments in the biological sample by post-sequencing *in silico* selection.