more cells. One recent study found a mean value of 37 fetal lymphocytes per milliliter of blood. (Huang, *Prenatal Diagnosis* 2008 28: 892-899).

[0008] Thus, there is a need for improved methods and tools for detecting fetal alleles and fetal genetic variations.

SUMMARY OF THE INVENTION

[0008a] In one aspect, the present disclosure refers to an *in vitro* method of obtaining and analyzing a fetal genome from a mixture of maternal and fetal cells, comprising:

enriching a sample comprising a mixture of maternal and fetal cells;

dividing said enriched sample into at least about 100 subsamples, wherein each subsample has an average of less than one cell;

performing whole genome amplification on each at least about 100 subsamples to provide an amplified product for each subsample, wherein each amplified product has an amplified genome from an average of about one cell;

dividing each of said amplified product into aliquots, wherein each aliquot contains at least one copy of said amplified genome from said cell;

screening or genotyping an aliquot for the presence of a fetal identifier, wherein said screening or genotyping comprises:

screening or genotyping said aliquot for a genotype differing from a maternal genotype at at least one target locus, wherein the presence of said genotype differing from said maternal genotype indicates the presence of an informative paternal allele in said aliquot;

identifying the presence of a fetal cell in at least one subsample whose aliquot contains an informative paternal allele; and

analyzing another aliquot from said at least one subsample identified as containing fetal cell to detect a genetic variation in said genome of said fetal cell.

[0009] Example~~embodiments~~ of the present disclosure~~invention~~ relate to methods and genotyping panels for detecting fetal alleles and fetal genetic variations. One example~~embodiment of the invention~~ is a method of detecting a fetal identifier, comprising: obtaining a sample comprising a mixture of maternal and fetal cells; dividing the sample into subsamples; screening or genotyping a subsample for the presence of a fetal identifier; and identifying the presence of at least one fetal identifier from a fetal cell in at least one subsample.

[0010] Example~~embodiments~~ of the disclosure~~invention~~ can and may comprise one or more of the following: a method further comprising performing subsample amplification on at least one subsample to provide an amplified product; a method further comprising dividing the amplified product into aliquots, where screening or genotyping a subsample for the presence of at least one fetal identifier comprises screening an aliquot for the presence of a fetal identifier; a method where subsample amplification comprises a method selected from the group consisting of: whole genome amplification, whole transcriptome amplification, targeted nucleic acid amplification, amplification of a nucleic acid sequence other than the fetal identifier, generation of a proxy for a nucleic acid sequence, and cell division; a method where preamplification comprises whole genome amplification or whole transcriptome amplification; a method where preamplification comprises targeted nucleic acid amplification, amplification of a nucleic acid sequence other than the fetal identifier, generation of a proxy for a nucleic acid sequence, and cell division; a method further comprising determining whether the genetic material of the maternal cells is homozygous or heterozygous at a set of target loci to determine a maternal genotype, where screening or genotyping an aliquot or subsample for a fetal identifier comprises screening or genotyping the aliquot or subsample for a genotype differing from the maternal genotype at at least one target locus, where the presence of the genotype differing from the maternal genotype indicates the presence of an informative paternal allele in the amplified product, and where identifying the presence of at least one fetal identifier comprises identifying an informative paternal

where the amplified product comprises genomic DNA or complementary DNA; a method where determining a maternal genotype comprises using a panel of SNPs to genotype a sample of maternal genetic material from the same individual that is the source of the maternal cells; a method where the source of the maternal genetic material is selected from the group consisting of blood, serum, plasma, urine, a cervical swab, tears, saliva, buccal swab, or skin; a method where the source of the maternal genetic material is selected from the group consisting of blood or a buccal swab; a method where the mixture of maternal and fetal nucleic acids is a mixture of cell-free nucleic acids; a method where the source of the maternal and fetal cell-free nucleic acid sample is blood, serum, plasma, urine, cervical swab, cervical lavage, uterine lavage, or culdocentesis from a pregnant female; a method comprising selecting and screening or genotyping more than one test locus in a single aliquot or subsample, selecting and screening or genotyping more than one test locus in more than one aliquot or subsample, or selecting and screening or genotyping one test locus in more than one aliquot or subsample; a method comprising selecting and screening or genotyping a second target locus in at least a second subsample following the identification of an informative paternal allele in a first aliquot or subsample; a method where the samples are divided to generate subsamples with a Poisson or a Non-Poisson distribution of cells; a method where each subsample comprises not more than one cell; a method further comprising pooling aliquots from two or more subsamples prior to screening or genotyping; a method where pooling comprises the use of an indexed system of rows and columns of wells comprising the aliquots; a method further comprising enriching the sample for the fetal cells prior to dividing into subsamples; a method where enriching comprises differential expansion of the fetal cells over the maternal cells; a method where a homogeneous portion of the amplified product is divided into the aliquots; and a method where a non-homogeneous portion of the amplified product is divided into the aliquots.

[0011] Yet another <u>example</u>~~embodiment of the invention~~ is a single nucleotide polymorphism (SNP) panel for detecting a fetal allele, comprising at least one chromosome-specific panel comprising about 5 to about 100 unique SNPs specific for a single chromosome, where each of the SNPs has a frequency in the range of about 30% to about 50% as measured across all major population groups; and where the total number of SNPs in the SNP panel is between about 5 and about 100 SNPs.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT