

CLAIMS

What is claimed is:

1. ~~— A method of enriching a sample for short nucleic acids of less than 300 nucleotides in length, the method comprising:~~

~~contacting the sample with polyethylene glycol in the presence of a monovalent salt under conditions suitable for substantially precipitating nucleic acids of 300 or greater nucleotides in length, without substantially precipitating the short nucleic acids; and~~

~~recovering the short nucleic acids.~~

2. ~~— A method of producing one or more target amplicons comprising one or more nucleotide tags from a sample, the method comprising:~~

~~preamplifying the one or more target nucleic acids in the sample with a first, outer primer pair to produce one or more first target amplicon(s); and~~

~~preamplifying the one or more target amplicon(s) with a second primer pair, wherein one or both primers of the second primer pair anneals to a primer binding site in between the primer binding sites of the outer primer pair, and~~

~~wherein at least one of the first, outer primer pair and/or the second primer pair comprises a nucleotide tag.~~

31. A method of enriching a sample for short nucleic acids of less than 300 nucleotides in length, the method comprising:

circularizing the sample nucleic acids under conditions that favor the circularization of short nucleic acids; and

recovering the circularized nucleic acids.

42. The method of claim 31 wherein said circularizing is carried out by contacting the sample nucleic acids with a circligase.

5. ~~— A method for tagging long nucleic acids and removing long nucleic acids of greater than 200 nucleotides in length, the method comprising:~~

~~contacting nucleic acids in the sample with a transposase in a reaction mixture under conditions suitable for fragmenting and tagging nucleic acids of greater than 200 nucleotides in length with transposon ends; and~~

~~selecting and removing transposon-tagged nucleic acids from the reaction mixture by affinity selection.~~

~~6. — The method of claim 5, wherein the conditions are suitable for fragmenting and tagging nucleic acids of greater than 300 nucleotides in length with transposon ends.~~

~~73.~~ The method of any of the preceding claims, additionally comprising the nucleic acids amplification and/or DNA sequencing to detect and/or quantify target nucleic acids within the recovered~~short~~ nucleic acids ~~or the tagged target amplicons~~.

~~84.~~ The method of any of the preceding claims, wherein the sample is unfractionated prior to enrichment.

~~95.~~ The method of any of the preceding claims, wherein the sample comprises a sample of a bodily fluid, or a fraction thereof, from a cancer patient.

~~106.~~ The method of any of the preceding claims, wherein the sample comprises a sample of a maternal bodily fluid, or a fraction thereof, from a pregnant subject.

~~117.~~ The method of claim ~~106~~, wherein at least some of the recovered~~short~~ nucleic acids comprise fetal DNA.

~~128.~~ The method of claim ~~106~~, wherein the maternal bodily fluid is selected from the group consisting of whole blood, plasma, urine, and cervico-vaginal secretions.

~~139.~~ The method of claim ~~106~~, wherein the method comprises determining a fetal genotype.

~~1410.~~ The method of claim ~~106~~, wherein the method comprises detecting the presence of a mutation or fetal aneuploidy.