

## CLAIMS

### WHAT IS CLAIMED IS:

1. A method for identifying a sample mismatch, comprising:
  - obtaining a first biological sample comprising a first plurality of nucleic acid molecules from a subject;
  - processing, by a computer, the first plurality of nucleic acid molecules to generate a first sample fingerprint comprising a quantitative measure of the first plurality of nucleic acid molecules at each of a plurality of genetic loci, wherein the plurality of genetic loci comprises autosomal single nucleotide polymorphisms (SNPs), wherein processing the first plurality of nucleic acid molecules comprises sequencing the first plurality of nucleic acid molecules to generate a first plurality of sequencing reads, and wherein the quantitative measure of the first plurality of nucleic acid molecules comprises a coverage of the first plurality of nucleic acid molecules at each of the plurality of genetic loci;
  - obtaining a second biological sample comprising a second plurality of nucleic acid molecules from the subject;
  - processing, by a computer, the second plurality of nucleic acid molecules to generate a second sample fingerprint comprising a quantitative measure of the second plurality of nucleic acid molecules at each of the plurality of genetic loci, wherein processing the second plurality of nucleic acid molecules comprises sequencing the second plurality of nucleic acid molecules to generate a second plurality of sequencing reads, and wherein the quantitative measure of the second plurality of nucleic acid molecules comprises a coverage of the second plurality of nucleic acid molecules at each of the plurality of genetic loci;
  - determining a difference between the first sample fingerprint and the second sample fingerprint; and
  - identifying the sample mismatch when the difference between the first sample fingerprint and the second sample fingerprint exceeds a pre-determined threshold,
  - wherein the autosomal single nucleotide polymorphisms comprise simple single nucleotide polymorphisms that have only two alleles that have no insertions or deletions.
2. The method of claim 1, wherein the autosomal single nucleotide polymorphisms have a minor allele fraction that exceeds about 7.5%.
3. The method of any of claims 1-2, wherein the first plurality of nucleic acid molecules and the second plurality of nucleic acid molecules comprise cell-free DNA (cfDNA), buffy coat DNA, or solid tumor DNA.

4. The method of any of claims 1-2, wherein the second biological sample is obtained from the subject at a later time after obtaining the first biological sample.
5. The method of any of claims 1-4, further comprising enriching the first plurality of nucleic acid molecules and/or the second plurality of nucleic acid molecules for at least a portion of the plurality of genetic loci.
6. The method of claim 5, wherein the enrichment comprises amplifying at least a portion of the first plurality of nucleic acid molecules and/or the second plurality of nucleic acid molecules.
7. The method of claim 6, wherein the amplification comprises selective amplification or universal amplification.
8. The method of claim 5, wherein the enrichment comprises selectively isolating at least a portion of the first plurality of nucleic acid molecules and/or the second plurality of nucleic acid molecules.
9. The method of any of claims 1-2, wherein the plurality of genetic loci comprises at least about 50 or at least about 100 distinct autosomal single nucleotide polymorphisms (SNPs).
10. The method of any of claims 1-9, comprising identifying the sample mismatch with a sensitivity or specificity of at least about 90%.
11. The method of any of claims 1-9, comprising identifying the sample mismatch with a positive predictive value (PPV) of at least about 90%, a negative predictive value (NPV) of at least about 90%, or an area under the curve (AUC) of at least about 0.90.
12. The method of any of claims 1-9, wherein the predetermined threshold is that the difference comprises a difference in genotype similarity greater than a predetermined threshold.
13. The method of claim 12, wherein the predetermined threshold is about 0.8.
14. The method of any of claims 1-13, further comprising excluding the second biological sample from further assaying based on the identified sample mismatch.
15. The method of any of claims 1-2, further comprising identifying a sample match when the difference between the first sample fingerprint and the second sample fingerprint does not satisfy the predetermined threshold.
16. The method of claim 15, comprising identifying the sample match with a sensitivity of at least about 90%, a specificity of at least about 90%, a positive predictive value (PPV) of at least about 90%, a negative predictive value (NPV) of at least about 90%, or an area under the curve (AUC) of at least about 0.90.
17. The method of any of claims 15-16, further comprising: (a) subjecting the second biological sample to further assaying based on the identified sample match; or (b) based on the

identified sample match, storing the second sample fingerprint in a database, and optionally, storing the first sample fingerprint in the database.

18. The method of claim 2, wherein the autosomal single nucleotide polymorphisms have a minor allele fraction that exceeds a predetermined threshold.

19. A non-transitory computer-readable medium comprising machine-executable code that, upon execution by one or more computer processors, implements a method for identifying a sample mismatch, comprising:

- receiving information of a first sample fingerprint comprising a quantitative measure of a first plurality of nucleic acid molecules of a first biological sample at each of a plurality of genetic loci, wherein the first sample fingerprint comprises a first plurality of sequencing reads obtained by sequencing the first plurality of nucleic acid molecules, wherein the quantitative measure of the first plurality of nucleic acid molecules comprises a coverage of the first plurality of nucleic acid molecules at each of the plurality of genetic loci, and wherein the plurality of genetic loci comprises autosomal single nucleotide polymorphisms (SNPs) that comprise simple single nucleotide polymorphisms that have only two alleles that have no insertions or deletions;

- receiving information of a second sample fingerprint comprising a quantitative measure of a second plurality of nucleic acid molecules of a second biological sample at each of the plurality of genetic loci, wherein the second sample fingerprint comprises a second plurality of sequencing reads obtained by sequencing the second plurality of nucleic acid molecules, wherein the quantitative measure of the second plurality of nucleic acid molecules comprises a coverage of the second plurality of nucleic acid molecules at each of the plurality of genetic loci, and wherein the second biological sample is obtained from the subject;

- determining a difference between the first sample fingerprint and the second sample fingerprint; and

- identifying the sample mismatch when the difference between the first sample fingerprint and the second sample fingerprint satisfies a predetermined threshold.

20. A system, comprising:

- one or more processors;

- a non-transitory computer-readable medium comprising machine-executable code that, upon execution by the one or more processors, implements a method for identifying a sample mismatch, comprising:

- receiving information of a first sample fingerprint comprising a quantitative measure of a first plurality of nucleic acid molecules of a first biological sample at each

of a plurality of genetic loci, wherein the first sample fingerprint comprises a first plurality of sequencing reads obtained by sequencing the first plurality of nucleic acid molecules, wherein the quantitative measure of the first plurality of nucleic acid molecules comprises a coverage of the first plurality of nucleic acid molecules at each of the plurality of genetic loci, and wherein the plurality of genetic loci comprises autosomal single nucleotide polymorphisms (SNPs) that comprise simple single nucleotide polymorphisms that have only two alleles that have no insertions or deletions;

receiving information of a second sample fingerprint comprising a quantitative measure of a second plurality of nucleic acid molecules of a second biological sample at each of the plurality of genetic loci, wherein the second sample fingerprint comprises a second plurality of sequencing reads obtained by sequencing the second plurality of nucleic acid molecules, wherein the quantitative measure of the second plurality of nucleic acid molecules comprises a coverage of the second plurality of nucleic acid molecules at each of the plurality of genetic loci, and wherein the second biological sample is obtained from the subject;

determining a difference between the first sample fingerprint and the second sample fingerprint; and

identifying the sample mismatch when the difference between the first sample fingerprint and the second sample fingerprint satisfies a predetermined threshold.