CLAIMS

1. A method comprising:

(a) obtaining a sample comprising a plurality of cell-free nucleic acid molecules, the plurality of cell-free nucleic acid molecules comprising a plurality of cell-free RNA molecules from a biological sample of an individual or a plurality of DNA molecules complementary to the plurality of cell-free RNA molecules;

(b) obtaining a panel of nucleic acid molecules that enriches for nucleic acids from a subset of a whole exome, wherein the subset comprises at least 5% of target genes identified in Table 3, wherein the target genes are rarely abundant as cell-free RNA transcripts within a plurality of control liquid biopsies; and

(c) enriching from the sample for the nucleic acids by contacting the sample with the panel of nucleic acid molecules.

2. The method of claim 1, wherein the panel of nucleic acid molecules enriches for at least 30% of the target genes identified in Table 3.

3. The method of claim 1 or 2, wherein the panel of nucleic acid molecules enriches for genes associated with:

(i) a plurality of tissue types, optionally wherein the plurality of tissue types comprises two or more members selected from bladder, kidney, liver, lung, pancreas, prostate, and breast;

(ii) a plurality of cell types; or

(iii) a plurality of cancer types, optionally wherein the plurality of cancer types comprises two or more members selected from lung adenocarcinomas (LUAD), pancreatic adenocarcinoma (PAAD), prostate adenocarcinoma (PRAD), and hepatocellular carcinoma (LIHC).

4. The method of any one of claims 1-4, wherein the panel of nucleic acid molecules enriches for lung cancer-associated genes or bladder cancer-associated genes.

5. The method of claim 1, wherein the panel of nucleic acid molecules is a set of nucleic acid probes for targeted capture hybridization or a set of nucleic acid primers for targeted amplification.

6. The method of any one of claims 1-5, wherein the panel of nucleic acid molecules lacks platelet-associated genes.

7. The method of any one of claims 1-6, further comprising:

generating sequencing read data of the nucleic acids; and

aligning the sequencing read data to a reference database to identify at least one member of the target genes; optionally wherein the at least one member comprises a plurality of members of the target genes.

8. The method of claim 7, further comprising determining a gene expression profile of the at least one member of the target genes based on the aligning.

9. The method of claim 8, wherein the individual is known to have a biological condition, and wherein the method further comprises (i) comparing the gene expression profile to a control gene expression profile of cell-free RNA libraries from a cohort of control subjects and (ii) identifying at least one gene that is differentially expressed in the individual as compared to the cohort of control subjects; optionally wherein the biological condition is cancer.

10. The method of claim 8 or 9, further comprising determining a presence of a gene expression signature within the gene expression profile, wherein the gene expression signature is indicative of the individual's likelihood of having a biological condition; optionally wherein the biological condition is cancer.

11. The method of claim 10, wherein the determining the presence of the gene expression signature comprises generating an enrichment score of at least one predetermined gene within the gene expression profile; optionally wherein the at least one predetermined gene comprises a plurality of predetermined genes.

12. The method of any one of claims 8-11, further comprising excluding, *in silico*, a gene expression contribution of platelets from the gene expression profile.

13. The method of any one of claims 7-12, further comprising identifying, based at least in part on the at least one member of the target genes:

(i) a somatic alteration selected from a single nucleotide variant (SNV), an insertion or deletion (indel), a gene fusion, and a splice variant;

(ii) a mechanism of resistance to a treatment for the individual; or

(iii) a biological condition of the individual; optionally wherein the biological condition is cancer.

14. The method of claim 13, further comprising determining, based at least in part on the at least one member of the target genes:

(i) the individual's response to a treatment for the biological condition; or

(ii) a treatment strategy for the biological condition of the individual.

15. The method of any one of claims 7-14, further comprising analyzing, via a machine learning model, a gene expression profile of the at least one member of the target genes, a somatic alteration derived from the at least one member of the target genes, or both to determine the individual's likelihood of having a biological condition; optionally wherein the machine learning model is based on elastic net, random forest, XGBoost, or neural network.