measurements. Ostroff, R. et al. (2010) J. Proteomics 73:649-666, documents some of the complex and nonlinear effects of variations in serum and plasma preparation.

**[0005]** Specific techniques to determine compliance with sample processing protocols are needed to monitor compliance, reject low quality samples, and/or make corrections in analytes of interest. Such techniques would improve evaluation of the quality of human or animal blood samples used in biomarker research, clinical diagnostic applications, bio-banks, and drug development.

## SUMMARY

**[0006]** The present application includes biomarkers, methods, reagents, devices, systems, and kits for assessing sample quality. The biomarkers of the present application were identified using linear regression of measurements of a specific set of proteins affected by variation in sample processing protocol. In some embodiments, the biomarker panels comprise proteins that are sensitive to sample handling.

**[0006a]** In one aspect, the present invention provides a method of assessing quality of a sample collected from a subject comprising detecting the level of each of N biomarker proteins in the sample, wherein N is at least 1, and wherein at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 of the N biomarker proteins are selected from LKHA4, EIF1B, RAGP1, SCFD1, PLD3, Lectin, mannose-binding 2, ILK1, and RPL5, wherein the sample is a serum sample.

**[0006b]** In one aspect, the present invention provides a method comprising:

a) measuring the level of each of N biomarker proteins in a serum sample from a subject, wherein N is at least 1, and wherein at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 of the N biomarker proteins are selected from LKHA4, EIF1B, RAGP1, SCFD1, PLD3, Lectin, mannose-binding 2, ILK1, and RPL5; and

b) identifying the sample as an analysis sample or negative sample based on the level of the N biomarker proteins;

wherein the analysis sample is a sample that is suitable for use in one or more of the following: protein biomarker discovery analysis, protein expression level analysis, a diagnostic method, or a prognostic method, and the negative sample is a sample that is not suitable for use as an analysis sample.

**[0006c]** In one aspect, the present invention provides a method comprising:

a) contacting a serum sample from a subject with a set of capture reagents, wherein each capture reagent has affinity for a different biomarker protein of N biomarker proteins

wherein N is at least 1, and wherein at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 of the N biomarker proteins is selected from LKHA4, EIF1B, RAGP1, SCFD1, PLD3, Lectin, mannose-binding 2, ILK1, and RPL5; and

b) measuring the level of each N biomarker protein with the set of capture reagents.

**[0006d]** In one aspect, the present invention provides a method for comparing a plurality of samples collected from a plurality of subjects comprising detecting the level of each of N biomarker proteins in each of the plurality of samples, wherein N is at least 1, and wherein at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 of the N biomarker proteins is selected from LKHA4, EIF1B, RAGP1, SCFD1, PLD3, Lectin, mannose-binding 2, ILK1, and RPL5, wherein the sample is a serum sample.

**[0006e]** In one aspect, the present invention provides a kit comprising N biomarker protein capture reagents, wherein N is at least 1, and wherein at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 of the capture reagents bind to proteins selected from LKHA4, EIF1B, RAGP1, SCFD1, PLD3, Lectin, mannose-binding 2, ILK1, and RPL5.

**[0006f]** In one aspect, the present invention provides a method comprising detecting the level of each of at least 1, 2, 3, 4, 5, 6, 7, or 8 biomarker proteins in a sample, wherein the biomarker proteins are selected from LKHA4, EIF1B, RAGP1, SCFD1, PLD3, Lectin, mannose-binding 2, ILK1, and RPL5.

**[0007]** In some embodiments, the methods comprise detecting the biomarkers using a multiplex slow off-rate aptamer-based assay described herein, for example, for assessing sample quality. In some embodiments, the sample is a blood sample, plasma sample, serum sample, or urine sample. In some embodiments, the sample is a plasma sample or a serum sample.

**[0008]** In some embodiments, the number of times a sample is frozen and thawed (freeze-thaw cycle) is predicted or estimated. In some embodiments, the sample processing steps include one or more of sample centrifugation, decanting or aspirating of the centrifuged supernatant, and freezing the decanted or aspirated sample.

**[0009]** In some embodiments, methods of assessing quality of a sample collected from a subject are provided, the method comprising detecting the level of each of N biomarker proteins in the sample, wherein N is at least 1, and wherein at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 of the N biomarker proteins are selected from LKHA4, EIF1B, RAGP1, SCFD1, PLD3, Lectin, mannose-binding 2, ILK1, and RPL5, wherein the sample is a serum sample.

**[0010]** In some embodiments, methods comprises measuring the level of each of N biomarker proteins in a serum sample from a subject are provided, wherein N is at least 1, and wherein at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 of the N biomarker proteins are selected from LKHA4, EIF1B, RAGP1, SCFD1, PLD3, Lectin, mannose-binding 2, ILK1, and RPL5, and identifying the sample as an analysis sample or