SUMMARY OF THE DISCLOSURE

[0007] The present disclosure relates generally to methods for determining and predicting pain. More particularly, the present disclosure relates to methods for objectively determining pain intensity, predicting future emergency department (ED) visits for pain. Also disclosed are methods for identifying drug and natural compounds as candidates for treating pain using biomarker gene expression signatures.

~~[0007a] In one aspect, the present disclosure is directed to a treatment for example selected from the group listed in Tables 1, 2A, 2B and 7 and combinations thereof for use in a method for treating pain in a subject in need thereof, the method comprising: obtaining an expression level of one or more blood biomarker(s) personalized by gender and diagnosis in a sample obtained from the subject; obtaining a reference expression level of the blood biomarker(s); identifying a difference in the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s); wherein the treatment is to be administered to reduce the difference between the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s) to mitigate pain in the subject.~~

[0008] The present disclosure is directed to a method for determining pain intensity in a subject in need thereof. The method comprises: obtaining an expression level of a blood biomarker in a sample obtained from the subject; obtaining a reference expression level of a blood biomarker; and identifying a difference between the expression level of the blood biomarker in a sample obtained from the subject and the reference expression level of a blood biomarker, wherein the difference in the expression level of the blood biomarker in the sample obtained from the subject and the reference expression level of the blood biomarker determines pain intensity. In another aspect, the present disclosure is directed to a method for determining intensity of pain, the method comprising: obtaining an expression level of one or more blood biomarker(s) personalized by gender and diagnosis in a sample obtained from a subject; obtaining a reference expression level of the blood biomarker(s); and identifying a difference in the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s), wherein the difference in the expression level of the blood biomarker(s) in the sample obtained from the subject and the reference expression level of the blood biomarker(s) determines the intensity of pain for example wherein the biomarker(s) is/are selected from the group of biomarkers listed in Table 1 and combinations thereof. In one example, the

reference expression level of the blood biomarkers; wherein the difference in the expression level of the blood biomarkers in the sample obtained from the subject and the reference expression level of the blood biomarkers determines the likelihood of future ED visits for pain. In one example, the blood biomarker is a panel of blood biomarkers. The reference expression level can be that as described herein.

[0010a] In another aspect, the present disclosure is directed to a method for predicting a future medical care facility visit for pain, the method comprising: obtaining an expression level of one or more blood biomarker(s) personalized by gender and diagnosis in a sample obtained from a subject; obtaining a reference expression level of the blood biomarker(s); identifying a difference in the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s), wherein the difference in the expression level of the blood biomarker(s) in the sample obtained from the subject and the reference expression level of the blood biomarker(s) determines the likelihood of future medical facility visits for pain for example wherein the biomarker(s) is/are selected from the group of biomarkers listed in Table 1 and combinations thereof.

[0011] The present disclosure is directed to a method for mitigating pain in a subject in need thereof. The method comprises: obtaining an expression level of a blood biomarker in a sample obtained from the subject; obtaining a reference expression level of the blood biomarker; identifying a difference in the expression level of the blood biomarker in the sample and the reference expression level of the blood biomarker; and administering a treatment, wherein the treatment reduces the difference between the expression level of the blood biomarker in the sample and the reference expression level of the blood biomarker to mitigate pain in the subject. ~~In another aspect, the present disclosure is directed to a treatment for example selected from the group listed in Tables 1, 2A, 2B and 7, and combinations thereof for use in a method for mitigating pain in a subject in need thereof, the method comprising: obtaining an expression level of one or more blood biomarker(s) personalized by gender and diagnosis in a sample obtained from the subject; obtaining a reference expression level of the blood biomarker(s); identifying a difference in the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s); and wherein the treatment is to be administered to reduce the difference between the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s) to mitigate pain in the subject.~~ In one

CLAIMS

What is claimed is:

~~1. A treatment for example selected from the group listed in Tables 1, 2A, 2B and 7 and combinations thereof for use in a method for treating pain in a subject in need thereof, the method comprising: obtaining an expression level of one or more blood biomarker(s) personalized by gender and diagnosis in a sample obtained from the subject; obtaining a reference expression level of the blood biomarker(s); identifying a difference in the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s); wherein the treatment is to be administered to reduce the difference between the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s) to mitigate pain in the subject.~~

~~2. The treatment for use according to claim 1, wherein the biomarker(s) is/are selected from the group consisting of microfibril associated protein 3 (MFAP3), phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Delta (PIK3CD), Sushi, Von Willebrand Factor Type A, EGF And Pentraxin Domain Containing 1 (SVEP1), TNF Receptor Superfamily Member 11b (TNFRSF11B), ElaC Ribonuclease Z 2 (ELAC2), and combinations thereof.~~

~~3. The treatment for use according to claim 1, wherein the biomarker(s) is decreased in response to the treatment.~~

~~4. The treatment for use according to claim 1, wherein the biomarker(s) is increased in response to the treatment.~~

~~5~~1. A method ~~for~~ of determining intensity of pain, the method comprising: obtaining an expression level of one or more blood biomarker(s) personalized by gender and diagnosis in a sample obtained from a subject; obtaining a reference expression level of the blood biomarker(s); and identifying a difference in the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s), wherein the difference in the expression level of the blood biomarker(s) in the sample obtained from the subject and the reference expression level of the blood biomarker(s) determines the intensity of pain for example wherein the biomarker(s) is/are selected from the group of biomarkers listed in Table 1 and combinations thereof.

~~6~~2. The method of claim ~~5~~1, wherein the biomarker(s) is/are selected from the group consisting of microfibril associated protein 3 (MFAP3), phosphatidylinositol-4,5-Bisphosphate

3-Kinase Catalytic Subunit Delta (PIK3CD), Sushi, Von Willebrand Factor Type A, EGF And Pentraxin Domain Containing 1 (SVEP1), TNF Receptor Superfamily Member 11b (TNFRSF11B), ElaC Ribonuclease Z 2 (ELAC2), and combinations thereof.

~~7~~3. The method of claim ~~5~~1, wherein the expression level of the blood biomarker(s) in the sample obtained from the subject is increased as compared to the reference expression level of the biomarker(s).

~~8~~4. The method of claim ~~5~~1, wherein the expression level of the blood biomarker(s) in the sample obtained from the subject is decreased as compared to the reference expression level of the biomarker(s).

~~9~~5. A method of ~~for~~ predicting a future medical care facility visit for pain, the method comprising: obtaining an expression level of one or more blood biomarker(s) personalized by gender and diagnosis in a sample obtained from a subject; obtaining a reference expression level of the blood biomarker(s); identifying a difference in the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s), wherein the difference in the expression level of the blood biomarker(s) in the sample obtained from the subject and the reference expression level of the blood biomarker(s) determines the likelihood of future medical facility visits for pain for example wherein the biomarker(s) is/are selected from the group of biomarkers listed in Table 1 and combinations thereof.

~~10~~6. The method of claim ~~9~~5, wherein the expression level of the blood biomarker(s) in the sample obtained from the subject is increased as compared to the reference expression level of the biomarker(s).

~~11~~7. The method of claim ~~9~~5, wherein the expression level of the blood biomarker(s) in the sample obtained from the subject is decreased as compared to the reference expression level of the biomarker(s).

~~12. A treatment for example selected from the group listed in Tables 1, 2A, 2B and 7, and combinations thereof for use in a method for mitigating pain in a subject in need thereof, the method comprising: obtaining an expression level of one or more blood biomarker(s) personalized by gender and diagnosis in a sample obtained from the subject; obtaining a reference expression level of the blood biomarker(s); identifying a difference in the expression level of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s); and wherein the treatment is to be administered to reduce the difference between the expression level~~

~~of the blood biomarker(s) in the sample and the reference expression level of the blood biomarker(s) to mitigate pain in the subject.~~

~~13. The treatment for use according to claim 12, wherein the treatment is selected from the group consisting of SC-560, pyridoxine, methylergometrine, LY-294002, haloperidol, cytisine, cyanocobalamin, betaescin, amoxapine, apigenin and combinations thereof.~~

~~14. The treatment for use according to claim 12, wherein the treatment is selected from the group listed in Table 2B, and combinations thereof.~~

~~15~~8. A method of ~~for~~ identifying one or more blood biomarker(s) for pain personalized by gender and diagnosis, the method comprising: identifying a first cohort of subjects by identifying subjects having a change from low pain intensity to high pain intensity as determined by a difference between the first pain intensity test and the second pain intensity test; identifying candidate biomarkers in the first cohort by identifying biomarker(s) having a change in expression between the first biological sample and the second biological sample that had been obtained from the subject.

~~16~~9. The method of claim ~~15~~ 8 further comprising prioritizing the candidate biomarker(s) by identifying candidate biomarker(s) known to be associated with pain.

~~17~~10. The method of claim ~~15~~8, wherein the pain intensity test is selected from the group consisting of Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP), and combinations thereof.