a) measuring a first or activity of 51 kDa FK506 binding protein (FKBP5 protein) in a first sample obtained from the subject, wherein said measuring consists of measuring FKBP5 protein peptidyl-prolyl-cis-trans isomerase activity in the sample or of measuring FKBP5 binding activity by measuring the amount of FKBP5 protein bound to glucocorticoid receptor (GR) in the sample, and wherein:

i) the first sample comprises primary cells; and

ii) the first sample is obtained before the GRA is administered to the subject;

b) measuring a second activity of FKBP5 protein in a second sample obtained from the subject, wherein said measuring consists of measuring FKBP5 protein peptidyl-prolyl-cis-trans isomerase activity in the sample or of measuring the amount of FKBP5 protein bound to glucocorticoid receptor (GR) in the sample, and wherein:

i) the second sample comprises primary cells; and

ii) the second sample is obtained after the GRA is administered to the subject; and

c) comparing the first and second activities,

wherein a reduction in the activity of FKBP5 protein in the second sample indicates the biochemical response to the GRA.

**[0003b]** In yet another aspect of the present disclosure, there is provided an in vitro method for assessing a biochemical response in a human subject to administering to the subject a medical or surgical therapy for treatment of hypercortisolemia, the method comprising:

a) measuring a first activity of 51 kDa FK506 binding protein (FKBP5 protein) in a first sample obtained from the subject, wherein said measuring consists of measuring FKBP5 protein peptidyl-prolyl-cis-trans isomerase activity in the sample or of measuring FKBP5 binding activity by measuring the amount of FKBP5 protein bound to glucocorticoid receptor (GR) in the sample, and wherein:

i) the first sample comprises primary cells; and

ii) the first sample is obtained before administering the medical or surgical therapy for treatment of hypercortisolemia to the subject;

b) measuring a second activity of FKBP5 protein in a second sample obtained from the subject, wherein said measuring consists of measuring FKBP5 protein peptidyl-prolyl-cis-trans isomerase activity in the sample or of measuring the amount of FKBP5 protein bound to glucocorticoid receptor (GR) in the sample, and wherein:

i) the second sample comprises primary cells; and

ii) the second sample is obtained after the medical or surgical therapy for treatment of hypercortisolemia is administered to the subject; and

c) comparing the first and second amounts, activities, or expression levels,

wherein a reduction in the activity of FKBP5 protein in the second sample indicates the biochemical response to the medical or surgical therapy for treatment of hypercortisolemia.

**[0004]** The present disclosure provides a method for assessing a clinical or biochemical response to a glucocorticoid receptor antagonist (GRA) in a human subject, the method comprising: a) measuring a first amount, or activity of 51 kDa FK506 binding protein

WHAT IS CLAIMED IS:

1. An in vitro method for assessing a biochemical response to a glucocorticoid receptor antagonist (GRA) in a human subject, the method comprising:

a) measuring a first activity of 51 kDa FK506 binding protein (FKBP5 protein) in a first sample obtained from the subject, wherein said measuring consists of measuring FKBP5 protein peptidyl-prolyl-cis-trans isomerase activity in the sample or of measuring FKBP5 binding activity by measuring the amount of FKBP5 protein bound to glucocorticoid receptor (GR) in the sample, and wherein:

i) the first sample comprises primary cells; and

ii) the first sample is obtained before the GRA is administered to the subject;

b) measuring a second activity of FKBP5 protein in a second sample obtained from the subject, wherein said measuring consists of measuring FKBP5 protein peptidyl-prolyl-cis-trans isomerase activity in the sample or of measuring the amount of FKBP5 protein bound to glucocorticoid receptor (GR) in the sample, and wherein:

i) the second sample comprises primary cells; and

ii) the second sample is obtained after the GRA is administered to the subject; and

c) comparing the first and second activities, wherein a reduction in the activity of FKBP5 protein in the second sample indicates the biochemical response to the GRA.

2. The in vitro method of claim 1, wherein the first sample is obtained prior to administering multiple doses of GRA to the subject, and the second sample is obtained after administering the multiple doses of GRA to the subject.

3. The in vitro method of claim 1 or 2, wherein the GRA administered to the subject comprises mifepristone.

4. The in vitro method of claim 1 or 2, wherein the GRA administered to the subject is not mifepristone.

5. The in vitro method of claim 4, wherein the GRA administered to the subject comprises a heteroaryl-ketone GRA.

6. The in vitro method of any of claims 1 to 5, wherein the first or second samples comprise whole blood, or a fraction thereof, or wherein the first or second samples comprise nasal epithelial scraping samples, or wherein the first and second samples comprise whole blood, or a fraction thereof.

7. The in vitro method of any of claims 1 to 6, wherein the patient a) is in need of administration of the glucocorticoid receptor antagonist (GRA); b) has elevated levels of cortisol; or c) has cancer and the first and second samples comprise tumor cells.

8. The in vitro method of claim 1, wherein the first and second samples comprise whole blood, or a fraction thereof.

9. The in vitro method of any of claims 1 to 8, wherein the method comprises administering an increased amount of GRA to the subject in the absence of a detected reduction in the activity of FKBP5 protein in the second sample.

10. An in vitro method for assessing a biochemical response in a human subject to administering to the subject a medical or surgical therapy for treatment of hypercortisolemia, the method comprising:

a) measuring a first activity of 51 kDa FK506 binding protein (FKBP5 protein) in a first sample obtained from the subject, wherein said measuring consists of measuring FKBP5 protein peptidyl-prolyl-cis-trans isomerase activity in the sample or of measuring FKBP5 binding activity by measuring the amount of FKBP5 protein bound to glucocorticoid receptor (GR) in the sample, and wherein:

i) the first sample comprises primary cells; and

ii) the first sample is obtained before administering the medical or surgical therapy for treatment of hypercortisolemia to the subject;

b) measuring a second activity of FKBP5 protein in a second sample obtained from the subject, wherein said measuring consists of measuring FKBP5 protein peptidyl-prolyl-cis-trans isomerase activity in the sample or of measuring the amount of FKBP5 protein bound to glucocorticoid receptor (GR) in the sample, and wherein:

i) the second sample comprises primary cells; and

ii) the second sample is obtained after the medical or surgical therapy for treatment of hypercortisolemia is administered to the subject; and

c) comparing the first and second amounts, activities, or expression levels,

wherein a reduction in the activity of FKBP5 protein in the second sample indicates the biochemical response to the medical or surgical therapy for treatment of hypercortisolemia.

11. The in vitro method of claim 10, wherein the medical or surgical therapy for treatment of hypercortisolemia is selected from the group consisting of: inhibition of steroidogenesis, administration of an ACTH modulator, GRA administration, transsphenoidal surgery, repeat transsphenoidal surgery, unilateral adrenalectomy, bilateral adrenalectomy, radiotherapy, resection of a non-pituitary ACTH-secreting tumor, treatment with a peptide receptor radionuclide therapy, and combinations thereof, wherein the method comprises administering an additional medical or surgical therapy for treatment of hypercortisolemia in an absence of a detected reduction in the amount or activity of FKBP5 protein or reduction in the expression level of the gene encoding FKBP5 protein in the second sample.