

particular therapy for SLE or LN, so that the need for utilizing the shotgun approach of treating with powerful immunosuppressive and chemotherapeutic agents may be reduced or eliminated. The present disclosure addresses these deficiencies.

SUMMARY OF THE INVENTION

[0013] The present disclosure relates methods of treating inflammatory or autoimmune diseases or disorders (such as SLE or LN) in certain subsets of subjects that are determined to be candidates for a particular treatment. Specific embodiments relate to methods of treating inflammatory or autoimmune diseases or disorders (such as SLE or LN) in certain subsets of subjects that are determined to be candidates for treatment with an inhibitor of the CD6-ALCAM pathway.

[0014] In some embodiments, the present invention provides a method for identifying whether a subject has a form of lupus nephritis that is sensitive to CD6-ALCAM pathway inhibition. ~~The method comprises determining whether the subject exhibits an elevated level of soluble CD6 and/or ALCAM protein;~~

~~(a) obtaining a urine sample from the subject and~~
~~(b) performing an assay on the urine sample to determine if soluble urine CD6 and/or soluble urine ALCAM protein in the sample is present at a concentration of 50,000 to 200,000 pg/ml,~~

~~wherein, if the soluble urine CD6 and/or soluble urine ALCAM protein in the sample is present at a concentration range of 50,000 to 200,000 pg/ml, then the subject has lupus nephritis.~~

[0015] In some embodiments, the present invention provides a method for treating lupus nephritis with a CD6-ALCAM pathway inhibitor, the method comprising:

(a) determining whether a biological sample obtained from a subject having or suspected of having lupus nephritis contains an elevated level of soluble CD6 and/or ALCAM protein; and

(b) administering to the subject a CD6-ALCAM pathway inhibitor if the biological sample contains an elevated level of soluble CD6 and/or ALCAM protein.

[0016] In some embodiments, the present invention provides ~~a method for using a~~ CD6-ALCAM pathway inhibitor ~~for use in treating to treat a subject with lupus nephritis.~~ ~~The use comprises the method comprising the steps of:~~

(a) determining whether ~~the subject exhibits elevated levels of soluble~~ urine CD6 and/or soluble urine ALCAM protein ~~in the subject is present at a concentration of between 50,000 to 200,000 pg/ml; and~~

(b) administering to the subject the CD6-ALCAM pathway inhibitor if the ~~subject exhibits elevated levels of soluble urine~~ CD6 and/or soluble urine ALCAM protein is present at a concentration of between 50,000 to 200,000 pg/ml.

[0017] In some embodiments, the present invention provides a method for treating a subject with a CD6-ALCAM pathway inhibitor, wherein the subject has lupus nephritis, the method comprising the steps of:

(a) determining whether the subject has a CD6-ALCAM pathway inhibitor- sensitive disease by:

(b) obtaining or having obtained a biological sample from the subject; and

(c) performing or having performed an assay on the biological sample to determine if the sample exhibits an elevated level of soluble CD6 and/or ALCAM protein; and

(d) administering the CD6-ALCAM pathway inhibitor to the subject if the subject has elevated soluble CD6 and/or ALCAM protein.

[0018] In some embodiments, the present invention provides a method for identifying whether a subject has an inflammatory or autoimmune disease that is sensitive to CD6- ALCAM pathway inhibition, the method comprising determining whether the subject exhibits an elevated level of soluble CD6 and/or ALCAM protein.

[0019] In some embodiments, the present invention provides a method for treating an inflammatory or autoimmune disease with a CD6-ALCAM pathway inhibitor, the method comprising:

(a) determining whether a biological sample obtained from a subject having or suspected of having inflammatory or autoimmune disease contains an elevated level of soluble CD6 and/or ALCAM protein; and

(b) administering to the subject a CD6-ALCAM pathway inhibitor if the biological sample contains an elevated level of soluble CD6 and/or ALCAM protein.

[0020] In some embodiments, the present invention provides a method for using a CD6-ALCAM pathway inhibitor to treat a subject with an inflammatory or autoimmune disease, the method comprising the steps of:

(a) determining whether the subject exhibits elevated soluble CD6 and/or ALCAM protein; and

(b) administering to the subject the CD6-ALCAM pathway inhibitor if the subject exhibits elevated soluble CD6 and/or ALCAM protein.

[0021] In some embodiments, the present invention provides a method for treating a subject with a CD6-ALCAM pathway inhibitor, wherein the subject has inflammatory or autoimmune

mycophenolate and cyclophosphamide.

[0041] In some embodiments, the present invention provides a method of predicting the prognosis of a subject with lupus nephritis. ~~The method comprising~~ comprises the steps of:

(a) obtaining ~~or having obtained~~ a plurality of ~~biological urine~~ samples from the subject over a time course of days, weeks, months or years; and

(b) performing or having performed an assay on each of the ~~biological urine~~ samples to determine if there is a change over time in the level of soluble urine CD6 and/or soluble urine ALCAM proteins that are present in the sample; wherein

(i) if the soluble urine CD6 and/or soluble urine ALCAM proteins in the sample exhibits an increase in the level of soluble CD6 and/or ALCAM protein presents at a concentration of more than 50,000 pg/ml over time, then the prognosis is determined to be poor;

(ii) if the sample exhibits no change in the level of soluble urine CD6 and/or soluble urine ALCAM protein over time, then the prognosis is determined to be neutral; and

(iii) if the soluble urine CD6 and/or soluble urine ALCAM proteins in the sample exhibits a decrease in the level of soluble CD6 and/or ALCAM protein presents at a concentration of less than 50,000 pg/ml over time, then the prognosis is determined to be good.

[0042] In some embodiments, the present invention provides a method of predicting the prognosis of a subject with an inflammatory or autoimmune disease, the method comprising the steps of:

(a) obtaining or having obtained a plurality of biological samples from the subject over a time course of days, weeks, months or years; and

(b) performing or having performed an assay on each of the biological samples to determine if there is a change over time in the level of soluble CD6 and/or ALCAM proteins that are present in the sample; wherein

(i) if the sample exhibits an increase in the level of soluble CD6 and/or ALCAM protein over time, then the prognosis is determined to be poor;

(ii) if the sample exhibits no change in the level of soluble CD6 and/or ALCAM protein over time, then the prognosis is determined to be neutral; and

(iii) if the sample exhibits a decrease in the level of soluble CD6 and/or ALCAM protein over time, then the prognosis is determined to be good.

[0043] In some embodiments, the present invention provides a method of determining whether a subject has active lupus nephritis. ~~The method comprises~~ comprising:

(a) determining a first concentration of soluble urine CD6 and/or soluble urine ALCAM protein present in a sample from the subject;

(b) determining a second concentration, or average concentration, of soluble urine CD6 and/or soluble urine ALCAM protein present in a similar sample from a control person, or a population of control persons, respectively, that do not have active lupus nephritis; and

(c) determining that the subject has active lupus nephritis if the first concentration is greater than the second concentration.

[0044] In some embodiments, the present invention provides a method of determining whether a subject has active inflammatory or autoimmune disease comprising

(a) determining a first concentration of soluble CD6 and/or ALCAM protein present in a sample from the subject;

(b) determining a second concentration, or average concentration, of soluble CD6 and/or ALCAM protein present in a similar sample from a control person, or a population of control persons, respectively, that do not have active lupus nephritis; and

(c) determining that the subject has active nephritis if the first concentration is greater than the second concentration.

[0045] In some embodiments, the present invention provides a method of determining whether a subject has transitioned from inactive lupus nephritis to active lupus nephritis. The method comprises comprising:

(a) determining a first concentration of soluble urine CD6 and/or soluble urine ALCAM protein present in a first sample from the subject; wherein the first sample is obtained from the subject when the subject has inactive lupus nephritis;

(b) determining a second concentration of soluble urine CD6 and/or soluble urine ALCAM protein present in one or more second samples from the subject; wherein each second sample is obtained from the subject after the first sample was obtained; and

(c) determining that the subject has active lupus nephritis or is transitioning into active nephritis if the second concentration of soluble urine CD6 and/or soluble urine ALCAM protein is greater than the first concentration.

[0046] In some embodiments, the present invention provides a method of determining whether a subject has transitioned from inactive inflammatory or autoimmune disease to active inflammatory or autoimmune disease comprising

(a) determining a first concentration of soluble CD6 and/or ALCAM protein present in a first sample from the subject; wherein the first sample is obtained from the subject when the subject has inactive lupus nephritis;

CLAIMS

1. ~~A method for using a CD6-ALCAM pathway inhibitor for use in treating to treat a subject with an inflammatory kidney disease~~ lupus nephritis, the ~~method use~~ comprising the steps of:

a. ~~determining whether the subject exhibits elevated levels of soluble~~ urine CD6 and/or soluble urine ALCAM protein in the subject is present at a concentration of between 50,000 to 200,000 pg/ml; and

b. ~~administering to the subject the CD6-ALCAM pathway inhibitor if the subject exhibits elevated levels of soluble~~ urine CD6 and/or soluble urine ALCAM protein is present at a concentration of between 50,000 to 200,000 pg/ml.

~~2. The method according to claim 1 wherein the inflammatory kidney disease is selected from the group comprising: lupus nephritis, IgA nephropathy, anti-neutrophil cytoplasmic antibody associated glomerulonephritis, autoimmune membranous nephropathy, anti glomerular basement membrane glomerulonephritis, and C3 nephropathy.~~

~~3.2. The CD6-ALCAM pathway inhibitor of claim 1~~ method of any one of claims 1-2, wherein the CD6-ALCAM pathway inhibitor is an anti-CD6 antibody, or the antigen binding fragment thereof.

~~4.3. The CD6-ALCAM pathway inhibitor of claim 2~~ method according to claim 3, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, is a humanized antibody.

~~5.4. The CD6-ALCAM pathway inhibitor of claim 3~~ method of claim 4, wherein the humanized antibody is itolizumab.

~~6.5. The CD6-ALCAM pathway inhibitor of any one of claims 2 to 4~~ method of any one of claims 3-5, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises heavy and light chain variable regions comprising amino acid sequences as set forth in SEQ ID NOs: 1 and 2.

~~7.6. A method for identifying whether a subject has an inflammatory kidney disease~~ lupus nephritis that is sensitive to CD6-ALCAM pathway inhibition, the method comprising:

a. obtaining a ~~biological~~ urine sample from the subject and

b. performing an assay on the ~~biological-urine~~ sample to determine if ~~the sample exhibits an elevated level of soluble~~ urine CD6 and/or soluble urine ALCAM protein in the sample is present at a concentration of 50,000 to 200,000 pg/ml;

wherein, if the soluble urine CD6 and/or soluble urine ALCAM protein in the sample is present at a concentration range of 50,000 to 200,000 pg/ml, then the subject has lupus nephritis.

~~8.7.~~ The method according to claim ~~76~~, wherein the ~~level-concentration of the~~ soluble urine CD6 and/or soluble urine ALCAM protein is determined in a first and one or more second sample from the subject.

~~9.8.~~ The method according to claim ~~87~~, wherein ~~the elevated level a~~ a higher concentration of the soluble urine CD6 and/or soluble urine ALCAM protein in the second sample with respect to the first sample indicates active disease in the subject.

~~10.9.~~ The method according to claim ~~87~~, wherein a ~~decrease in the level~~ lower concentration of the soluble urine CD6 and/or soluble urine ALCAM protein in the second sample with respect to the first sample indicates transition from an active disease to a passive disease in the subject.

~~11.—~~ The method according to claim ~~8~~, wherein a ~~threshold increase in the level of soluble~~ CD6 and/or ALCAM protein in the second sample as compared to the first sample indicates transition from a passive disease to an active disease in the subject.—

~~12.10.~~ A method of predicting the prognosis of a subject with ~~an inflammatory kidney disease~~ lupus nephritis, the method comprising the steps of:

i. obtaining a plurality of ~~biological-urine~~ samples from the subject over a time course of days, weeks, months or years; and

ii. performing or having performed an assay on each of the ~~biological-urine~~ samples to determine if there is a change over time in the level of soluble urine CD6 and/or soluble urine ALCAM proteins that are present in the sample; wherein

a. if the soluble urine CD6 and/or soluble urine ALCAM proteins in the sample ~~exhibits an increase in the level of soluble CD6 and/or ALCAM protein~~ presents at a concentration of more than 50,000 pg/ml over time, then the prognosis is determined to be poor;

b. if the sample exhibits no change in the level of soluble urine CD6 and/or soluble urine ALCAM protein over time, then the prognosis is determined to be neutral; and

c. if the soluble urine CD6 and/or soluble urine ALCAM proteins in the sample
~~exhibits a decrease in the level of soluble CD6 and/or ALCAM protein presents at a concentration~~
of less than 50,000 pg/ml over time, then the prognosis is determined to be good.

~~13.11.~~ A method of determining whether a subject has active lupus nephritis comprising

- a. determining a first concentration of soluble urine CD6 and/or soluble urine ALCAM protein present in a sample from the subject;
- b. determining a second concentration, or average concentration, of soluble urine CD6 and/or soluble urine ALCAM protein present in a similar sample from a control person, or a population of control persons, respectively, that do not have active lupus nephritis; and
- c. determining that the subject has active lupus nephritis if the first concentration is greater than the second concentration.

~~14.12.~~ A method of determining whether a subject has transitioned from inactive lupus nephritis to active lupus nephritis comprising

- a. determining a first concentration of soluble urine CD6 and/or soluble urine ALCAM protein present in a first sample from the subject; wherein the first sample is obtained from the subject when the subject has inactive lupus nephritis;
- b. determining a second concentration of soluble urine CD6 and/or soluble urine ALCAM protein present in one or more second samples from the subject; wherein each second sample is obtained from the subject after the first sample was obtained; and
- c. determining that the subject has active lupus nephritis or is transitioning into active nephritis if the second concentration of soluble urine CD6 and/or soluble urine ALCAM protein is greater than the first concentration.

~~15.13.~~ The method of any one of claims 13-14, further comprising an antibody for use in treating a subject with lupus nephritis, wherein

the antibody is itolizumab, and
the antibody is administered to the subject ~~administering to the subject the itolizumab antibody~~
~~antibody~~ if the subject has active lupus nephritis or is transitioning into active lupus nephritis.