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(54) Titre : METHODES DE DIAGNOSTIC, DE CLASSIFICATION ET DE PREDICTION DU RISQUE DE
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UN TRAITEMENT

(54) Title: METHODS FOR DIAGNOSING, STAGING, PREDICTING RISK FOR DEVELOPING AND IDENTIFYING
TREATMENT RESPONDERS FOR RHEUMATOID ARTHRITIS

(57) **Abrégé/Abstract:**

Disclosed are methods for diagnosing, staging, and predicting risk for developing rheumatoid arthritis and other inflammatory diseases, and methods for identifying treatment responders and non-responders.

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(54) Title: METHODS FOR DIAGNOSING, STAGING, PREDICTING RISK FOR DEVELOPING AND IDENTIFYING TREATMENT RESPONDERS FOR RHEUMATOID ARTHRITIS

(57) Abstract: Disclosed are methods for diagnosing, staging, and predicting risk for developing rheumatoid arthritis and other inflammatory diseases, and methods for identifying treatment responders and non-responders.

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**Methods for Diagnosing, Staging, Predicting Risk for Developing and Identifying
Treatment Responders for Rheumatoid Arthritis**

[0001] This application claims the benefit of U.S. Provisional Patent Application Serial No. 61/332,081, filed May 6, 2010; U.S. Provisional Patent Application Serial No. 61/428,500, filed December 30, 2010; and U.S. Provisional Patent Application Serial No. 61/444,702, filed February 19, 2011. Each of the above-referenced applications are incorporated by reference herein in their entirety.

[0002] Background

Rheumatoid Arthritis (RA) is characterized by synovial inflammation and destruction of joint cartilage and bone. Such destruction is caused in part by the ongoing synthesis of proinflammatory cytokines and matrix metalloproteinases. Autoimmune diseases, such as RA have been classically viewed as Th1 (CD4⁺ T helper cell-induced; interferon-gamma, for example, is produced, which activates the bactericidal activities of macrophages and induces B-cells to make opsonizing (coating) antibodies, leading to cellular immunity) and not Th2 (CD4⁺ T helper cell-induced; interleukin 4, for example, is released, which results in the activation of B-cells to make neutralizing antibodies, leading to humoral immunity) disorders. However, recent studies have brought this thought into questions (Lubberts; Seminars in Immunopathology 32(1), 43–53 (2010)). For example, IL-17a (a proinflammatory cytokine) is present at sufficient concentrations in the synovial fluid of RA patient joints that it can be detected. However, this and other cytokines cannot be detected in serum or plasma obtained from the same patients. There is a need to detect biomarkers in serum or plasma that are related to RA and other inflammatory disorders (e.g., Crohn's Disease, Inflammatory Bowel Disease (IBD), ulcerative colitis, psoriasis, Chronic Obstructive Pulmonary Disease (COPD)) so that RA can be more readily or effectively diagnosed and staged, risk for developing RA or other inflammatory disorder can be more readily or effectively assessed, and patients who are responders and non-responders to RA therapy can be more readily or effectively identified.

[0003] Summary of the Invention

[0004] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorders (e.g., Crohn's Disease, Inflammatory Bowel Disease (IBD), ulcerative colitis, psoriasis, Chronic Obstructive Pulmonary Disease (COPD)) in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A (Interleukin 17A), IL-17A/F (Interleukin 17A/17F heterodimer), and IL-17F (Interleukin 17F), and optionally one or more of IL-1 β (Interleukin 1-beta), IL-6 (Interleukin 6), totMMP-9 (total precursor and active matrix metalloproteinase 9 (or gelatinase B)), proMMP-9 (precursor protein of matrix metalloproteinase 9), cTnI (cardiac troponin I), and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and/or IL-17F greater than about 0.18 pg/ml, 1.35 pg/ml and 116 pg/ml, respectively, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorders. In certain aspects, subject IL-17A, IL-17A/F and/or IL-17F biomarker concentrations are compared to average biomarker concentrations for healthy volunteers, and in aspects age- and/or gender-matched healthy volunteers, to predict whether they have a greater than normal risk of developing RA or other inflammatory disorders. In other aspects, additional biomarker (e.g., IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI) concentrations are determined and utilized to predict whether a subject has a greater than normal risk of developing RA or other inflammatory disorders. In some aspects values are used, and in others comparisons to average biomarker concentrations for healthy volunteers, and in aspects age- and/or gender-matched volunteers are utilized.

[0005] In another aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorders in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and/or IL-17F greater than about 0.18 pg/ml, 1.35 pg/ml and 116 pg/ml, respectively, the subject has an increased likelihood of developing RA or other inflammatory disorders. In certain aspects, subject IL-17A, IL-17A/F and/or IL-17F biomarker concentrations are compared to average biomarker concentrations for healthy volunteers, and in aspects age- and/or gender-matched healthy volunteers, to determine the likelihood of the subject developing RA. In other aspects, additional biomarker (e.g., IL-1 β , IL-6, totMMP-9,

proMMP-9, cTnI) concentrations are determined and utilized to determine the likelihood of the subject developing RA or other inflammatory disorders. In some aspects values are used, and in others comparisons to average biomarker concentrations for healthy volunteers, and in aspects age- and/or gender-matched volunteers are utilized.

[0006] In another aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the RA patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the RA or other inflammatory disorder patient, obtaining a second sample from the RA patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the RA patient has a first concentration of IL-17A, IL-17A/F and/or IL-17F greater than about 0.18 pg/ml, 1.35 pg/ml and 116 pg/ml, respectively, and a second concentration of IL-17A, IL-17A/F and/or IL-17F less than about 0.18 pg/ml, 1.35 pg/ml and 116 pg/ml, respectively, the RA or other inflammatory disorder patient is identified as RA or other inflammatory disorder patients who responds to therapy.

[0007] In another aspect, the disclosure provides methods for predicting the rate of inflammatory disease progression in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the concentration of none, one or more than one of IL-17A is greater than 0.18 pg/ml, IL-17-F is greater than 116 pg/ml, or IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of one, one or more or at least two of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, or IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a slow rate, medium rate or high rate of inflammatory disease progression.

[0008] In another aspect, the disclosure provides methods for predicting the likelihood of inflammatory disease remission in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample,

wherein when the concentration of none, one or more than one of IL-17A is greater than 0.18 pg/ml, IL-17-F is greater than 116 pg/ml, or IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of one, one or more or at least two of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, or IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a high likelihood, medium likelihood or a low likelihood of inflammatory disease remission.

[0009] In another aspect, the disclosure provides methods for determining the severity of inflammatory disease in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the concentration of one or more of IL-17A is greater than 0.18 pg/ml, IL-17-F is greater than 116 pg/ml, or IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of none, one, one or more, or two or more or one of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, or IL-6 is greater than 1.0 pg/ml, the subject is determined to have mild, moderate or severe inflammatory disease.

[0010] For all of the above aspects related to predicting the rate of inflammatory disease progression, predicting the likelihood of inflammatory disease remission, or determining the severity of inflammatory disease, the inflammatory disease is selected from the group consisting of RA, Crohn's Disease, IBD, ulcerative colitis, psoriasis, and COPD.

[0011] In certain aspects, subject IL-17A, IL-17A/F and/or IL-17F biomarker concentrations are compared to average biomarker concentrations for healthy volunteers, and in aspects age- and/or gender-matched healthy volunteers, to identify RA or other inflammatory disorder patients who respond to therapy. In other aspects, additional biomarker (e.g., IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI) concentrations are determined and utilized to identify RA or other inflammatory disorder patients who respond to therapy. In some aspects values are used, and in others comparisons to average biomarker concentrations for healthy volunteers, and in aspects age- and/or gender-matched volunteers are utilized.

[0012] In another aspect, the disclosure provide method for determining inflammatory disease in a patient. The method includes detecting the concentration of more or more the

following markers in a patient sample: IL-17A, IL-17F, IL-17A/F, IL-1 β , IL-6, totMMP-9, proMMP-9, and cTnI, comparing the level of the one or more markers to the level in a normal population of healthy volunteers; and determining that the patient has inflammatory disease when the concentration of IL-17A, IL-17F, IL-17A/F, IL-6, or cTnI are elevated relative to the normal population, or totMMP-9, proMMP-9, or IL-1 β are decreased relative to the normal population. In certain aspects, the disease is RA and the one or more markers include the combination of IL-17F & IL-17A, the combination of IL-17A and IL-17 A/F, or the combination of IL-17F and IL-17 A/F.

[0013] Other aspects and embodiments of the invention will become apparent to those of skill in the art in view of the following detailed description.

[0014] Brief Description of the Drawings

[0015] Figure 1 illustrates various biomarker levels in RA patients versus healthy volunteers. The three hash marks through each data set represent mean and one standard deviation above and below the mean. Concentrations of several markers are significantly elevated or attenuated in RA patients (P-values are indicated).

[0016] Figure 2 provides a larger-scale view of select results illustrated in Figure 1. The three hash marks through each data set represent mean and upper and lower quartile divisions (rather than mean and one standard deviation above and below the mean).

[0017] Figure 3 illustrates the heretofore unknown importance of the IL-17A, IL-17F, IL-17A/F heterodimer in RA biology. Only 6% of RA patients in the sample had neither IL-17A nor IL-17F present at elevated concentrations over HV. All RA patients had at least one of IL-17A, IL-17F, and IL-17A/F heterodimer present at elevated concentrations over HV.

[0018] Figure 4 shows box plots of the markers that best classify RA along with a box plot for TNF α .

[0019] Figure 5 shows that the combination of IL-17F & IL-17A as biomarkers for RA were 100% predictive of disease.

[0020] Figure 6 shows that the combination of IL-17A and IL-17 A/F as biomarkers for RA perform very well in predicting disease.

[0021] Figure 7 shows that the combination of IL-17F and IL-17 A/F as biomarkers for RA perform very well in predicting disease.

[0022] Detailed Description of the Invention

[0023] All publications, patent applications, patents and other references mentioned herein, if not otherwise indicated, are explicitly incorporated by reference.

[0024] Unless otherwise defined, the technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art. Expansion and clarification of some terms are provided herein.

[0025] As used herein, the term "subject" refers to a mammal that can be afflicted by a rheumatoid arthritis, but may or may not have such a disease. Typically, the terms "subject" and "patient" are used herein interchangeably in reference. In various embodiments, the subject is a human.

[0026] As used herein, the term "sample" is taken broadly to include any sample suitable for the methods described herein. Typically, the sample is a biological sample such as, for example, a biological fluid. Such fluids can include, without limitation, bronchoalveolar lavage fluid (BAL), blood, serum, plasma, urine, nasal swab, cerebrospinal fluid, pleural fluid, synovial fluid, peritoneal fluid, amniotic fluid, gastric fluid, lymph fluid, interstitial fluid, tissue homogenate, cell extracts, saliva, sputum, stool, physiological secretions, tears, mucus, sweat, milk, semen, seminal fluid, vaginal secretions, fluid from ulcers and other surface eruptions, blisters, and abscesses, and extracts of tissues including biopsies of normal, malignant, and suspect tissues or any other constituents of the body which may contain the target particle of interest. Other similar specimens such as cell or tissue culture or culture broth are also of interest. In some embodiments, the sample is a blood sample. In some embodiments the sample is a plasma sample. In some embodiments the sample is a serum sample.

[0027] As used herein, the term "healthy volunteer average concentrations" refers to the average concentration of the various biomarkers described herein for at least two subjects who do not have RA (e.g., HV). Preferably, average concentration values are calculated from biomarker concentrations measured in larger groups of HVs. Healthy volunteer average

concentrations are provided herein, but one of skill in the art may also measure biomarker concentrations in one or more populations of subjects lacking RA utilizing an apparatus capable of sensitively measuring the concentrations of biomarkers described herein and calculating the average values for each biomarker in such HV populations.

[0028] As used herein, the term “therapy” refers to the administration of any medical treatment (e.g., pharmaceuticals) or interventional treatment (e.g., surgery) to affect RA or the biomarkers relevant to RA described herein.

[0029] As used herein, the term “substantially the same as” refers to $\pm$ about 25%, $\pm$ about 20%, $\pm$ about 15%, $\pm$ about 10%, $\pm$ about 5%, $\pm$ about 3%, $\pm$ about 2%, or $\pm$ about 1% of the healthy volunteer average concentrations of a biomarker. In some aspects “substantially the same as” refers to $\pm$ about 20%, $\pm$ about 15%, $\pm$ about 10%, or $\pm$ about 5%, $\pm$ about 3%, $\pm$ about 2%, or $\pm$ about 1% of the healthy volunteer average concentrations of a biomarker. In some aspects “substantially the same as” refers to $\pm$ about 15%, $\pm$ about 10%, $\pm$ about 5%, $\pm$ about 3%, $\pm$ about 2%, or $\pm$ about 1% of the healthy volunteer average concentrations of a biomarker. In some aspects “substantially the same as” refers to $\pm$ about 10%, $\pm$ about 5%, $\pm$ about 3%, $\pm$ about 2%, or $\pm$ about 1% of the healthy volunteer average concentrations of a biomarker. In some aspects “substantially the same as” refers to $\pm$ about 5%, $\pm$ about 3%, $\pm$ about 2%, or $\pm$ about 1% of the healthy volunteer average concentrations of a biomarker. In some aspects “substantially the same as” refers to $\pm$ about 3%, $\pm$ about 2%, or $\pm$ about 1% of the healthy volunteer average concentrations of a biomarker. In some aspects “substantially the same as” refers to $\pm$ about 2%, or $\pm$ about 1% of the healthy volunteer average concentrations of a biomarker. In some aspects “substantially the same as” refers to $\pm$ about 1% of the healthy volunteer average concentrations of a biomarker.

[0030] As used herein, the term “CV” refers to the coefficient of variance. In some aspects “substantially the same as” refers to $\pm$ about 10%, $\pm$ about 5%, $\pm$ about 3%, $\pm$ about 2%, or $\pm$ about 1% of the healthy volunteer average concentrations of a biomarker. In some aspects “substantially the same as” refers to $\pm$ about 5%, $\pm$ about 3%, $\pm$ about 2%, or $\pm$ about 1% of the healthy volunteer average concentrations of a biomarker.

[0031] As used herein, the term “average CV” refers to average of the coefficient of variance obtained for all samples tested in triplicate.

[0032] As used herein, the term “LoD” refers to the limit of detection, defined as 2 standard deviations above the zero calibrator.

[0033] As used herein, the term “LLOQ” refers to the lower limit of quantification, defined from data generated off of the standard curve. Specifically, the back interpolated values of standards in triplicate provide CVs < 20% and a bias <20% of the expected values.

[0034] As used herein, the terms “inflammatory disorder” and “inflammatory disease” refer to any of a number of conditions in which inflammation is increased over normal subjects. Non-limiting examples of inflammatory disorders are rheumatoid arthritis, Crohn’s Disease, Inflammatory Bowel Disease, ulcerative colitis, psoriasis, and Chronic Obstructive Pulmonary Disease (COPD).

[0035] The American College of Rheumatology has developed criteria to aid in determining the progression, remission, and functional status of patients with RA.

[0036] Progression of RA (clinical and radiologic staging) is classified as follows: Stage I (early RA) is characterized by no destructive changes observed upon roentgenographic examination; radiographic evidence of osteoporosis is possible. Stage II (moderate progression) is characterized by radiographic evidence of periarticular osteoporosis, with or without slight subchondral bone destruction; slight cartilage destruction is possible; joint mobility is possibly limited; no joint deformities are observed; adjacent muscle atrophy is observed; extra-articular soft-tissue lesions (eg, nodules, tenosynovitis) are possible. Stage III (severe progression) is characterized by radiographic evidence of cartilage and bone destruction in addition to periarticular osteoporosis; joint deformity (e.g., subluxation, ulnar deviation, hyperextension) without fibrous or bony ankylosis; extensive muscle atrophy; and extra-articular soft-tissue lesions (eg, nodules, tenosynovitis) are possible. Stage IV (terminal progression) is characterized by fibrous or bony ankylosis in addition to the criteria of Stage III.

[0037] Remission of RA is defined as ≥ 5 of the following conditions occurring for at least 2 consecutive months: duration of morning stiffness does not exceed 15 minutes; no fatigue; no joint pain; no joint tenderness or pain with motion; no soft-tissue swelling in joints or tendon sheaths; ESR (erythrocyte sedimentation rate) of less than 30 millimeters/hour (mm/h) in a female or less than 20 mm/h in a male.

[0038] Functional status of patients with RA is defined as follows: Class I individuals are completely able to perform usual activities of daily living. Class II individuals are able to perform usual self-care and vocational activities but limited in avocational activities. Class III individuals are able to perform usual self-care activities but limited in vocational and avocational activities. Class IV individuals are limited in ability to perform usual self-care, vocational, and avocational activities.

[0039] We hypothesized that the concentrations of many cytokines and matrix metalloproteinases in blood serum or plasma may parallel the relative abundance in inflamed joints of RA patients, and that a highly sensitive assay could be used to measure them. Further, we hypothesized that differences in cytokine concentrations could be determined between RA patients and otherwise healthy matched controls with such highly sensitive assays. Herein we describe the use of a highly sensitive immunoassay system to measure cytokines and other biomarkers in blood plasma obtained from RA patients and healthy control subjects and describe differences in biomarker concentrations that we have discovered between these two study groups. The measurement of differences in the biomarker concentrations, either up- or down-regulated, singly or in combination, in RA patients versus control subjects provides opportunities for better (e.g., simpler, earlier, faster) disease diagnosis, disease staging, risk classification, and/or identification of therapy responders/non-responders.

[0040] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0041] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations

thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0042] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0043] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0044] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than

about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0045] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0046] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0047] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-

17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing RA.

[0048] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0049] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0050] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations

thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0051] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0052] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing RA.

[0053] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations

thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0054] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0055] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0056] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F or

IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0057] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0058] In an aspect, the disclosure provides methods for predicting the risk for developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing RA or other inflammatory disorder.

[0059] For any of the above aspects related to predicting the risk for developing RA or other inflammatory disorder in a subject, the methods pertain to predicting the risk for developing RA.

[0060] For any of the above aspects related to predicting the risk for developing RA or other inflammatory disorder in a subject, the methods pertain to predicting the risk for developing Crohn's Disease.

[0061] For any of the above aspects related to predicting the risk for developing RA or other inflammatory disorder in a subject, the methods pertain to predicting the risk for developing Inflammatory Bowel Disease.

[0062] For any of the above aspects related to predicting the risk for developing RA or other inflammatory disorder in a subject, the methods pertain to predicting the risk for developing ulcerative colitis.

[0063] For any of the above aspects related to predicting the risk for developing RA or other inflammatory disorder in a subject, the methods pertain to predicting the risk for developing psoriasis.

[0064] For any of the above aspects related to predicting the risk for developing RA or other inflammatory disorder in a subject, the methods pertain to predicting the risk for developing Chronic Obstructive Pulmonary Disease (COPD).

[0065] In another aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0066] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than

about 116 pg/ml, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0067] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0068] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0069] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer

average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0070] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0071] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0072] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer

average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0073] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0074] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0075] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-

IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0076] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0077] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0078] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than

about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0079] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0080] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0081] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration

of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0082] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0083] In an aspect, the disclosure provides methods for determining the likelihood of developing RA or other inflammatory disorder in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing RA or other inflammatory disorder.

[0084] For any of the above aspects related to determining the likelihood of developing RA or other inflammatory disorder in a subject, the methods pertain to determining the likelihood of developing RA.

[0085] For any of the above aspects related to determining the likelihood of developing RA or other inflammatory disorder in a subject, the methods pertain to determining the likelihood of developing Crohn's Disease.

[0086] For any of the above aspects related to determining the likelihood of developing RA or other inflammatory disorder in a subject, the methods pertain to determining the likelihood of developing Inflammatory Bowel Disease.

[0087] For any of the above aspects related to determining the likelihood of developing RA or other inflammatory disorder in a subject, the methods pertain to determining the likelihood of developing ulcerative colitis.

[0088] For any of the above aspects related to determining the likelihood of developing RA or other inflammatory disorder in a subject, the methods pertain to determining the likelihood of developing psoriasis.

[0089] For any of the above aspects related to determining the likelihood of developing RA or other inflammatory disorder in a subject, the methods pertain to determining the likelihood of developing Chronic Obstructive Pulmonary Disease (COPD).

[0090] In another aspect, the disclosure provides methods for determining inflammatory disease in a patient. For example a number of markers can be used to diagnose existing inflammatory disease such as RA. Figures 1, 2, and 3 show that patients with elevated levels of IL-17A, IL-17F, and IL-17A/F, either alone or in combination, are likely to be suffering from RA. Other markers, such as IL-1 β , IL-6, totMMP-9, proMMP-9, and cTnI, are also useful in determining disease. Accordingly, in one aspect the disclosure provides a method of detecting inflammatory disease by measuring the amount of one or more of IL-17A, IL-17F, IL-17A/F, IL-1 β , IL-6, totMMP-9, proMMP-9, and cTnI, in a patient sample, comparing the sample to a control population, and determining whether a patient is suffering from inflammatory disease. Statistically significant differences between the patient sample and the control population (healthy volunteers) for one or more markers can be indicative of disease. As shown in Figure 3, only 6% of RA patients in the reference population had neither IL-17A nor IL-17F present at elevated concentrations over healthy volunteers (HV). All RA patients had at least one of IL-17A, IL-17F, and IL-17A/F heterodimer present at elevated concentrations over (HV). In particular embodiments, as shown in Figures 5, 6 and 7, the combination of IL-17F & IL-17A, the combination of IL-17A and IL-17 A/F, or the combination of IL-17F and IL-17 A/F can be used as biomarkers in diagnosing RA.

[0091] In another aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[0092] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml and of IL-17F of less than about 116 pg/ml, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[0093] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and

IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[0094] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml and of IL-17F of less than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 substantially the same as healthy

volunteer average concentrations for totMMP-9, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[0095] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[0096] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than

healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[0097] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, and a second concentration of one or more of IL-17A, IL-17A/F or IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F or IL-17F, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[0098] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, and a second concentration of IL-17A, IL-17A/F and IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F and IL-17F,

the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[0099] In an aspect, the disclosure provides methods for identifying RA or other an inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A, IL-17A/F or IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00100] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than healthy

volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A, IL-17A/F or IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00101] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A, IL-17A/F and IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00102] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F,

and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A, IL-17A/F and IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00103] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, or a concentration of

totMMP-9 greater than about 5.0 ng/ml, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00104] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, or a concentration of totMMP-9 greater than about 5.0 ng/ml, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00105] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116

pg/ml, in combination with a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00106] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml and of IL-17F of less than about 116 pg/ml, in combination with a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00107] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration

of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A, IL-17A/F or IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00108] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A, IL-17A/F or IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00109] In an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for

IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A, IL-17A/F and IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00110] an aspect, the disclosure provides methods for identifying an RA or other inflammatory disorder patient who responds to therapy, comprising obtaining a first sample from the patient, determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample, administering a therapy to the patient, obtaining a second sample from the patient, and determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample, wherein when the subject has a first concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A, IL-17A/F and IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the RA or other inflammatory disorder patient is identified as a patient who responds to therapy.

[00111] For any of the above aspects related to identifying an RA or other inflammatory disorder patient who responds to therapy, the methods pertain to identifying an RA patient who responds to therapy.

[00112] For any of the above aspects related to identifying an RA or other inflammatory disorder patient who responds to therapy, the methods pertain to identifying a Crohn's Disease patient who responds to therapy.

[00113] For any of the above aspects related to identifying an RA or other inflammatory disorder patient who responds to therapy, the methods pertain to identifying a Inflammatory Bowel Disease patient who responds to therapy.

[00114] For any of the above aspects related to identifying an RA or other inflammatory disorder patient who responds to therapy, the methods pertain to identifying an ulcerative colitis patient who responds to therapy.

[00115] For any of the above aspects related to identifying an RA or other inflammatory disorder patient who responds to therapy, the methods pertain to identifying a psoriasis patient who responds to therapy.

[00116] For any of the above aspects related to identifying an RA or other inflammatory disorder patient who responds to therapy, the methods pertain to identifying a COPD patient who responds to therapy.

[00117] In another aspect, the disclosure provides methods for predicting the rate of inflammatory disease progression in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the concentration of none or one of IL-17A is greater than 0.18 pg/ml, IL-17-F is greater than 116 pg/ml, or IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of one of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, or IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a slow rate of inflammatory disease progression.

[00118] In an aspect, the disclosure provides methods for predicting the rate of inflammatory disease progression, wherein when the concentrations of one of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, and the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of one or more of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a medium rate of inflammatory disease progression.

[00119] In an aspect, the disclosure provides methods for predicting the rate of inflammatory disease progression, wherein when the concentrations of one or more of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, and the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of at least two of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a high rate of inflammatory disease progression.

[00120] In another aspect, the disclosure provides methods for predicting the likelihood of inflammatory disease remission in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the concentration of none or one of IL-17A is greater than 0.18 pg/ml, IL-17-F is greater than 116 pg/ml, or IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of one of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, or IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a high likelihood of inflammatory disease remission.

[00121] In an aspect, the disclosure provides methods for predicting the likelihood of inflammatory disease remission in a subject, wherein when the concentrations of one of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, and the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of one or more of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a medium likelihood of inflammatory disease remission.

[00122] In an aspect, the disclosure provides methods for predicting the likelihood of inflammatory disease remission in a subject, wherein when the concentrations of one or more of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, and the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of at least two of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a low likelihood of inflammatory disease remission.

[00123] In another aspect, the disclosure provides methods for determining the severity of inflammatory disease in a subject, comprising obtaining a sample from the subject, determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample, wherein when the concentration of one of IL-17A is greater than 0.18 pg/ml, IL-17-F is greater than 116 pg/ml, or IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of none or one of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, or IL-6 is greater than 1.0 pg/ml, the subject is determined to have mild inflammatory disease.

[00124] In an aspect, the disclosure provides methods for determining the severity of inflammatory disease in a subject, wherein when the concentrations of at least one of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, or the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of one or more of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is determined to have moderate inflammatory disease.

[00125] In another aspect, the disclosure provides methods for determining the severity of inflammatory disease in a subject, wherein when the concentrations of at least one of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, and the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of two or more of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is determined to have severe inflammatory disease.

[00126] For any of the above aspects related to predicting the rate of inflammatory disease progression, predicting the likelihood of inflammatory disease remission, or determining the severity of inflammatory disease, the inflammatory disease is RA, Crohn's Disease, IBD, ulcerative colitis, psoriasis, or COPD.

[00127] For any of the above aspects related to predicting the rate of inflammatory disease progression, predicting the likelihood of inflammatory disease remission, or determining the severity of inflammatory disease, the inflammatory disease is RA.

[00128] For any of the above aspects related to predicting the rate of inflammatory disease progression, predicting the likelihood of inflammatory disease remission, or determining the severity of inflammatory disease, the inflammatory disease is Crohn's Disease.

[00129] For any of the above aspects related to predicting the rate of inflammatory disease progression, predicting the likelihood of inflammatory disease remission, or determining the severity of inflammatory disease, the inflammatory disease is IBD.

[00130] For any of the above aspects related to predicting the rate of inflammatory disease progression, predicting the likelihood of inflammatory disease remission, or determining the severity of inflammatory disease, the inflammatory disease is ulcerative colitis.

[00131] For any of the above aspects related to predicting the rate of inflammatory disease progression, predicting the likelihood of inflammatory disease remission, or determining the severity of inflammatory disease, the inflammatory disease is psoriasis.

[00132] For any of the above aspects related to predicting the rate of inflammatory disease progression, predicting the likelihood of inflammatory disease remission, or determining the severity of inflammatory disease, the inflammatory disease is COPD.

[00133] In various embodiments of the methods disclosed herein, concentrations of biomarkers related to RA or other inflammatory disorder comprise values that are elevated or reduced relative to the concentrations of those same biomarkers in a normal population of subjects (e.g., the HV group as provided herein). One of skill in the art may also measure biomarker concentrations in one or more HV populations utilizing an apparatus capable of sensitively measuring the concentrations of biomarkers described herein and calculate the average values for each biomarker in such HV populations.

[00134] In embodiments of the methods, the sample can be a single sample from the subject. In some embodiments, the sample can be a series of samples taken at various points in time so that changes in concentration over time of biomarker related to RA or other inflammatory disorder can be identified and interpreted. In embodiments, the samples can be taken in over the course of hours, days, weeks, months, and years. The samples can be taken at any regular or irregular interval based on the detected concentration(s) of biomarker related

to RA or other inflammatory disorder and/or the change in the concentration(s) of biomarker related to RA or other inflammatory disorder in the one or more samples over time.

[00135] In embodiments that track patient data and samples over time, such information can be taken from any known clinical study or database that maintains such patient samples and/or patient history.

[00136] Systems for Detection

[00137] As noted above, the diagnostic/prognostic methods described herein generally involve the determination of the amount of biomarker related to RA or other inflammatory disorder from one or a set of samples from a subject. Determination of concentrations of biomarker related to RA or other inflammatory disorder in the practice of the methods can be performed using any suitable apparatus or system that allow for the detection levels described herein. Such suitable apparatus, includes, but is not limited to, the systems described in Published U.S. Patent Application Nos: 2009/0159812 (Livingston); 2008/0003685 (Goix, et al.); and U.S. Patent 7,572,640, all incorporated herein by reference. U.S. Patent 7,572,640 describes instruments, reagents and methods for measuring analytes at levels to carry out this invention and thus identify those patients with of biomarker related to RA levels above or below the normal HV range.

[00138] Examples

[00139] Example 1:

[00140] The Erenna System, based upon Singulex Single Molecule Counting technology, was used for immunoassay analysis. This system has been described previously (Todd et al., Clin Chem. 53(11): 1990-1995 (2007); Todd et al., Clin Chem. 55(1):196-8 (2009); incorporated by reference). Immunoassays for the analytes described in the table below were constructed from commercially available antibodies and analytes. The immunoassay procedure used in the analyses of these analytes has been described previously as well (Todd et al., *supra*). All antibodies and analytes were obtained from R&D Systems (Minneapolis, MN) except for cTnI analyte, which was obtained from HyTest (Turku, Finland), and antibodies to cTnI, which were obtained from BiosPacific (Emeryville, CA). The volume of sample stated in Table 6 was added to a well in a 96 well plate, along with sufficient volume of calibrator diluent (3% BSA, Tris pH 8.0, 150 mM NaCl) to create a final volume of 100 ul for all test but for cTnI, which had a final volume of 50 ul. 100 ul of paramagnetic microparticles, and 150 ul for cTnI assays (MPs, MyOne, Invitrogen Dynal AS; approximately 5-10 ug MPs/well), coated with the capture antibody and diluted in assay buffer (1% BSA, Tris-buffered saline, pH 7.4, with 0.5 mL Triton X-100/L, and heterophile/human antimouse antibody–blocking reagents (from Scantibodies Laboratories, used per the manufacturer’s recommendations)), were added to each well and incubated for about 2 hours (about 1 hour for cTnI and IL-1 β). MPs were separated using a magnetic bed (Ambion). Supernatant was removed, MPs were washed once, and then 20 uL detection antibody (50–500 mg/L diluted in assay buffer) was added and incubated for about 1 hour at 25 °C with shaking. The MPs were again magnetically separated and washed 5 times using Tris-buffered saline with 0.5 mL Triton X-100/L. After removal of residual wash buffer, 20 uL elution buffer (Glycine pH 2.5) was added. This reagent disrupted antibody–analyte interactions and resulted in the release of detection antibody from the MPs. The solution in each 96-well plate was then transferred to a 384-well filter plate (0.2 um, AcroPrep cat. no. 5070, Pall) and centrifuged at 1200g for 3 minutes to separate detection antibody in elution buffer from MPs. The eluted and filtered material in the 384-well plate was then placed into the Erenna Immunoassay System. The concentration of biomarker in each sample was determined via interpolation off a standard curve run with the samples. For samples that used a volume less than 100 ul, the resulting interpolated values were adjusted and standardized to

a final sample volume of 100 ul (and 50 ul for cTnI). The value used to convert the standard into pg/mL was provided by the vendor.

[00141] All human serum specimens used in this study were obtained from ProMedDx (Norton, MA), and obtained under IRB approval and informed consent. All specimens were collected under protocol, which included noting time of blood collection into serum tubes, separation of serum from cells and storing of resulting serum at -70C. Healthy volunteers (HV) refers to serum collected from otherwise healthy subjects, age range of 42-73 years. Rheumatoid arthritis (RA) refers to serum collected from 17 clinically documented RA patients that had an average rheumatoid factor (RF) value of 75 IU/mL. Approximately 50% of the RA patients were on TNF- α inhibitors. The age range for these subjects was 42-80. 59% were males and 41% were females. Matched controls refers to subjects that were matched in age and sex to the RA subjects, but did not have RA.

[00142] Using highly sensitive immunoassays we were able to quantify the concentration of a variety of analytes in serum obtained from HV, RA subjects and matched controls (Figures 1, 2). The analytes described in Table 1 and Table 2 were measureable in all study subjects. Importantly, all of the assays had limits of quantification (CV <20%) that were lower than the concentration of the analytes measured in serum. This ensured that the measurement of analyte was accurate. We made the following observations:

[00143] Cardiac Troponin-I (cTnI) was elevated in a number of RA patients. Of note the elevations were modest (average approx 11 pg/mL) which was 3-4 fold higher than the average value found in the matched controls (approximately 3 pg/mL). 15/16 of these RA patients had cTnI concentrations < approximately 50 pg/mL, which is the limit of quantification for commercially available cTnI assays. Thus, this small increase (but significant in terms of exceeding the 99% normal range (at CV <10%) of cTnI of 7 pg/ml) in cTnI could not be noted with other assays.

[00144] IL-17F was elevated in RA patients compared to matched controls. This is the first time that anyone has found IL-17F to be elevated in RA.

[00145] IL-17A was found to be elevated in RA patients. Although the increase in IL-17A was modest (approximately 3-fold) it was highly statistically significant. This is the first time that IL-17A has been shown to be elevated in RA patients compared to controls in plasma and

furthermore the magnitude of the elevation was modest and at a low concentration (average approx 1 pg/mL).

[00146] Similar to IL-17A, heterodimer IL-17A/F was found elevated in RA patients. This is the first time that the concentrations of this heterodimer have been shown in blood serum from healthy volunteers, or serum from RA patients or matched controls.

[00147] IL-6 was found elevated in RA patients versus controls. It has been previously shown that IL-6 is elevated in RA patients; however, it has never been shown that IL-6 elevation correlates with elevations of IL-7A, IL-17F, IL-17A/F, and/or cTnI in some subjects and does not correlate with such elevations in other subjects.

[00148] IL-1 β was shown to be decreased in RA patients. This is the first time that this serum biomarker has been shown to be down-regulated in RA.

[00149] The measurement of differences in the biomarker concentrations, either up- or down-regulated, singly or in combination, in RA patients versus control subjects provides opportunities for better (e.g., simpler, earlier, faster) disease diagnosis, disease staging, risk classification, disease progression, disease severity and/or identification of therapy responders/non-responders.

[00150] **Table 1.** Comparison of biomarker concentrations in healthy volunteer (HV) blood donors and subjects with rheumatoid arthritis.

Biomarker	Unit	Healthy		RA		p-Value	Sample Volume (ul)
		Mean $\pm$ SD	Range	Mean $\pm$ SD	Range		
CRP	ng/mL	3.5 $\pm$ 3.0	0.8 - 8.8	11.4 $\pm$ 16.0	0.4 - 49.3	0.4188	0.0005
TNF RI	ng/mL	2.4 $\pm$ 0.6	1.4 - 3.7	2.5 $\pm$ 0.8	1.5 - 3.9	0.9142	0.1
TNF RII	ng/mL	6.2 $\pm$ 1.8	3.6 - 9.8	7.3 $\pm$ 2.5	3.7 - 13.1	0.2811	0.01
totMMP-9	ng/mL	5.1 $\pm$ 1.9	2.4 - 8.6	2.8 $\pm$ 1.6	0.9 - 7.1	0.0043	0.001
proMMP-9	ng/mL	1.0 $\pm$ 0.3	0.5 - 1.5	0.6 $\pm$ 0.4	0.2 - 1.3	0.0461	0.05
IL-1 RA	ng/mL	1.2 $\pm$ 0.4	0.7 - 2.0	0.8 $\pm$ 0.5	0.2 - 1.7	0.0753	10
TIMP-2	pg/mL	156 $\pm$ 16	140 - 192	156 $\pm$ 30	91 - 204	0.6273	0.01
MMP-2/TIMP2	pg/mL	76 $\pm$ 12	61 - 95	79 $\pm$ 15	43 - 105	0.4182	0.1
IL-17F	pg/mL	41 $\pm$ 32	16 - 116	579 $\pm$ 1002	63 - 3937	0.0002	10
TNF α	pg/mL	7.9 $\pm$ 1.6	5.9 - 11.0	16.4 $\pm$ 31.5	5.0 - 129.9	0.905	10
cTnI	pg/mL	2.3 $\pm$ 1.0	1.3 - 4.5	11.5 $\pm$ 23.1	1.3 - 95.9	0.1042	20

IL-6	pg/mL	1.7 ± 1.7	0.6 - 5.9	3.1 ± 2.3	0.7 - 7.0	0.0423	5
IL-1 β	pg/mL	2.2 ± 1.0	1.1 - 3.9	0.44 ± 0.18	0.25 - 0.90	0.0003	40
IL-17A	pg/mL	0.13 ± 0.03	0.07 - 0.18	0.36 ± 0.28	0.11 - 1.30	0.0033	100
IL-17A/F	pg/mL	0.73 ± 0.35	0.37 - 1.35	1.81 ± 1.73	0.56 - 7.14	0.0033	100
Note: one RA pt was excluded from the IL-1 β calculations due to the 99.99% probability of the value being an outlier (>4 SD from the mean; 30.11 pg/ml)							

[00151] Table 2. Comparison of biomarker concentrations in healthy volunteer (HV) blood donors and subjects with rheumatoid arthritis (median values).

Biomarker	Unit	Healthy Median	RA Median
CRP	ng/mL	2.62	3.79
TNF RI	ng/mL	2.34	2.35
TNF RII	ng/mL	6.23	7.05
totMMP-9	ng/mL	5.01	2.65
proMMP-9	ng/mL	0.96	0.68
IL-1 RA	ng/mL	1.25	0.55
TIMP-2	pg/mL	148	148
MMP-2/TIMP2	pg/mL	72	78
IL-17F	pg/mL	30.4	190
TNF α	pg/mL	7.5	7.6
cTnI	pg/mL	2.1	4.1
IL-6	pg/mL	1.0	2.0
IL-1 β	pg/mL	2.26	0.44
IL-17A	pg/mL	0.14	0.32
IL-17A/F	pg/mL	0.62	1.15

[00152] Table 3. Percent or fold change in plasma biomarker concentration for RA patients versus HV

	Healthy		RA			Mean change	% or fold change
Biomarker	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range	p-Value	HV to RA	HV to RA
totMMP-9	5.1 ± 1.9	2.4 - 8.6	2.8 ± 1.6	0.9 - 7.1	0.0043	-2.3	- 45%
proMMP-9	1.0 ± 0.3	0.5 - 1.5	0.6 ± 0.4	0.2 - 1.3	0.0461	-0.4	- 40%
IL-17F	41 ± 32	16 - 116	579 ± 1002	63 - 3937	0.0002	+538	+ 14-fold
cTnI	2.3 ± 1.0	1.3 - 4.5	11.5 ± 23.1	1.3 - 95.9	0.1042	+9.2	+ 4-fold
IL-6	1.7 ± 1.7	0.6 - 5.9	3.1 ± 2.3	0.7 - 7.0	0.0423	+1.4	+ 82%
IL-1 β	2.2 ± 1.0	1.1 - 3.9	0.44 ± 0.18	0.25 - 0.90	0.0003	- 1.76	- 80%

IL-17A	0.13 ± 0.03	0.07 - 0.18	0.36 ± 0.28	0.11 - 1.30	0.0033	+0.23	+ 2.8-fold
IL-17A/F	0.73 ± 0.35	0.37 - 1.35	1.81 ± 1.73	0.56 - 7.14	0.0033	+1.08	+ 2.5-fold
Note: one RA pt was excluded from the IL-1 β calculations due to the 99.99% probability of the value being an outlier (>4 SD from the mean; 30.11 pg/ml)							

[00153] Table 4. Raw biomarker concentration data, in pg/ml.

ID#	cTnI	IL-1b	IL-1 RA	TNF RI	TNF RII	TNFa	IL-6	IL-17F	IL-17A
HV1		1.26	709	1339	3624	8.1	1	31.2	0.14
HV2	4.5	3.87	1303	2126	4650	6.3	0.6	30.4	0.13
HV3	2.2	2.36	1512	2762	6742	8.5	1.7	26.8	0.14
HV4	2.7	1.34	756	1970	5210	6.8	1.1	71.2	0.15
HV5	1.7	3.67	2016	3727	9784	11	2.4	16	0.18
HV6	2.9	1.84	1253	2336	5445	5.9	0.7	20.1	0.07
HV7	1.6	1.06	758	2192	6443	7.5	0.8	33.3	0.16
HV8	1.3	2.54	1362	2485	6232	7.5	5.9	115.8	0.09
HV9	1.9	2.26	796	2426	7397	9.8	1.1	21.2	0.13
RA1	3	0.54	986	2351	5414	6.7	6.8	616.7	0.11
RA2	3.6	0.9	478	2998	7077	7.2	3.2	62.7	0.55
RA3	14.3	0.44	545	2583	7347	5.6	6.5	1417.3	0.51
RA4	5.9	0.38	748	2603	7638	10.6	2.7	139	0.18
RA5	1.3	0.35	341	1629	5211	7.6	2.2	121.5	0.42
RA6	1.6	0.54	1504	2368	7367	10.8	5.9	191.1	0.11
RA7		0.25	432	2273	6345	9.5	1.7	92.4	0.38
RA8	13.7	0.7	515	1815	5368	6.4	1.1	75.5	0.26
RA9	1.3	0.33	286	1870	5377	6.2	1.3	190.1	0.32
RA10	1.5	0.28	244	3853	10460	15.1	1	85.1	0.37
RA11	95.9	30.11	1717	3689	13119	129.9	7	3936.6	1.3
RA12	18.6	0.33	481	1549	3727	7.6	0.7	329.5	0.2
RA13	3.1	0.45	1533	1832	5464	7.4	2	883.2	0.12
RA14	4.5	0.73	842	1987	5612	5	1.2	143.3	0.51
RA15	1.8	0.33	890	3638	11348	10.4	3.3	395.2	0.37
RA16	4.6	0.38	382	3910	9643				0.26
RA17	8.6	0.62	1410	1984	7047				0.19

[00154] Table 5. Raw biomarker concentration data, in pg/ml, continued.

ID#	MMP2/ TIMP2	MMP-2	totMMP9	proMMP9	CRP	IL-17AF	RF
HV1	73	54	5239	955	7038	0.37	0
HV2	91	56	6994	1262	903	0.62	0
HV3	67	54	3200	582	4481	0.55	0
HV4	72	54	4236	776	2624	0.52	0
HV5	61	50	5006	942	8790	1.29	0
HV6	70	49	5517	1240	886	0.69	0
HV7	95	69	2377	508	770	0.67	0
HV8	85	58	8556	1493	1059	0.49	0
HV9	71	53	4843	1169	5291	1.35	0
RA1	67	46	7126	1154	8846	0.56	100
RA2	73	49	4691	995	19660	1.57	100
RA3	43	28	3347	1340	33972	1.55	100
RA4	78	56	2724	458	2483	1.13	100
RA5	75	53	4144	797	6812	0.71	86.2
RA6	66	53	3536	860	49340	0.9	68.9
RA7	71	53	1226	209	383	1.12	42.8
RA8	78	61	2329	663	4136	0.75	71
RA9	103	79	1212	157	1360	1.73	92.4
RA10	77	74	900	151	667	0.69	59
RA11	105	85	2690	656	44292	7.14	100
RA12	79	61	2608	742	1395	1.15	44.7
RA13	78	61	1251	277	3792	5.06	82.1
RA14	87	75	3986	993	1054	1.91	43.2
RA15	70	49	2652	733	14137	1.49	63.9
RA16	102	83	1467	173	944	0.91	28.69
RA17	92	74	1828	681	1014	2.39	100

[00155] Table 6 shows AuROC as a measure of predictive power for RA. AuROC does not depend on specifying a cut-point and can be interpreted as the probability that a random RA patient will be classified correctly. $\text{AuROC} > 0.8$ suggests very good performance. Odds ratios require specification of a somewhat arbitrary cut-point, wherein the large CIs show the uncertainty in the odds ratios caused by small sample size.

[00156] Table 6. AuROC analysis of RA biomarkers

Marker	AuROC	p-Value	Odds Ratio (95% CI)
IL-17F	0.941	0.0001	56 (3.3, 2700)
IL-17A	0.863	0.0018	16 (1.7, 208)
IL-17 A/F	0.863	0.0018	56 (3.3, 2700)
Total MMP-9	0.85	0.0029	0.088 (0.0072,0.79)
IL-6	0.735	0.051	5 (0.63,60)
TNFα	0.569	0.5967	3.1 (0.40, 38)

[00157] Although various specific embodiments of the present invention have been described herein, it is to be understood that the invention is not limited to those precise embodiments and that various changes or modifications can be affected therein by one skilled in the art without departing from the scope and spirit of the invention.

[00158] The examples given above are merely illustrative and are not meant to be an exhaustive list of all possible embodiments, applications or modifications of the invention. Thus, various modifications and variations of the described methods and systems of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with specific embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in molecular biology, immunology, chemistry, biochemistry or in the relevant fields are intended to be within the scope of the appended claims.

[00159] It is understood that the invention is not limited to the particular methodology, protocols, and reagents, etc., described herein, as these may vary as the skilled artisan will recognize. It is also to be understood that the terminology used herein is used for the purpose

of describing particular embodiments only, and is not intended to limit the scope of the invention.

[00160] Any numerical values recited herein include all values from the lower value to the upper value in increments of one unit provided that there is a separation of at least two units between any lower value and any higher value. As an example, if it is stated that the concentration of a component or value of a process variable such as, for example, size, angle size, pressure, time and the like, is, for example, from 1 to 90, specifically from 20 to 80, more specifically from 30 to 70, it is intended that values such as 15 to 85, 22 to 68, 43 to 51, 30 to 32, etc. are expressly enumerated in this specification. For values which are less than one, one unit is considered to be 0.0001, 0.001, 0.01 or 0.1 as appropriate. These are only examples of what is specifically intended and all possible combinations of numerical values between the lowest value and the highest value enumerated are to be considered to be expressly stated in this application in a similar manner.

[00161] Particular methods, devices, and materials are described, although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the invention. The disclosures of all references and publications cited herein are expressly incorporated by reference in their entireties to the same extent as if each were incorporated by reference individually.

We Claim:

1. A method for predicting the risk for developing an inflammatory disorder in a subject, comprising:

(a) obtaining a sample from the subject;

(b) determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample;

wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

2. The method of claim 1, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

3. The method of claim 1, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

4. The method of claim 1, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less

than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

5. The method of claim 1, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

6. The method of claim 1, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

7. The method of claim 1, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

8. The method of claim 1, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

9. The method of claim 1, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

10. The method of claim 1, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

11. The method of claim 1, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

12. The method of claim 1, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

13. The method of claim 1, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of

greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

14. The method of claim 1, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

15. The method of claim 1, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

16. The method of claim 1, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

17. The method of claim 1, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

18. The method of claim 1, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

19. The method of claim 1, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject is predicted to have a greater than normal risk of developing an inflammatory disorder.

20. A method for determining the likelihood of developing an inflammatory disorder in a subject, comprising:

- (a) obtaining a sample from the subject;
- (b) determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample;

wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, the subject has an increased likelihood of developing an inflammatory disorder.

21. The method of claim 20, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, the subject has an increased likelihood of developing an inflammatory disorder.

22. The method of claim 20, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater

than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing an inflammatory disorder.

23. The method of claim 20, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing an inflammatory disorder.

24. The method of claim 20, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing an inflammatory disorder.

25. The method of claim 20, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing an inflammatory disorder.

26. The method of claim 20, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, the subject has an increased likelihood of developing an inflammatory disorder.

27. The method of claim 20, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing an inflammatory disorder.

28. The method of claim 20, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing an inflammatory disorder.

29. The method of claim 20, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing an inflammatory disorder.

30. The method of claim 20, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, the subject has an increased likelihood of developing an inflammatory disorder.

31. The method of claim 20, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing an inflammatory disorder.

32. The method of claim 20, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing an inflammatory disorder.

33. The method of claim 20, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing an inflammatory disorder.

34. The method of claim 20, wherein when the subject has a concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing an inflammatory disorder.

35. The method of claim 20, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9

less than about 5.0 ng/ml, the subject has an increased likelihood of developing an inflammatory disorder.

36. The method of claim 20, wherein when the subject has a concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing an inflammatory disorder.

37. The method of claim 20, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing an inflammatory disorder.

38. The method of claim 20, wherein when the subject has a concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, the subject has an increased likelihood of developing an inflammatory disorder.

39. A method for identifying an inflammatory disorder patient who responds to therapy, comprising:

- (a) obtaining a first sample from the patient;
- (b) determining a first concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the first sample;
- (c) administering a therapy to the patient;
- (d) obtaining a second sample from the patient; and

(e) determining a second concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the second sample;

wherein when the inflammatory disorder patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, the inflammatory disorder patient is identified as a patient who responds to therapy.

40. The method of claim 39, wherein when the patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml and of IL-17F of less than about 116 pg/ml, the inflammatory disorder patient is identified as a patient who responds to therapy.

41. The method of claim 39, wherein when the patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the inflammatory disorder patient is identified as a patient who responds to therapy.

42. The method of claim 39, wherein when the patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater

than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml and of IL-17F of less than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the inflammatory disorder patient is identified as a patient who responds to therapy.

43. The method of claim 39, wherein when the patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the inflammatory disorder patient is identified as a patient who responds to therapy.

44. The method of claim 39, wherein when the patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9

substantially the same as healthy volunteer average concentrations for totMMP-9, the inflammatory disorder patient is identified as a patient who responds to therapy.

45. The method of claim 39, wherein when the patient has a first concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, and a second concentration of one or more of IL-17A, IL-17A/F or IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F or IL-17F, the inflammatory disorder patient is identified as a patient who responds to therapy.

46. The method of claim 39, wherein when the patient has a first concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, and a second concentration of IL-17A, IL-17A/F and IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F and IL-17F, the inflammatory disorder patient is identified as a patient who responds to therapy.

47. The method of claim 39, wherein when the patient has a first concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A, IL-17A/F or IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the inflammatory disorder patient is identified as a patient who responds to therapy.

48. The method of claim 39, wherein when the patient has a first concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer

average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A, IL-17A/F or IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the inflammatory disorder patient is identified as a patient who responds to therapy.

49. The method of claim 39, wherein when the patient has a first concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A, IL-17A/F and IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, or a concentration of totMMP-9 substantially the same as healthy volunteer average concentrations for totMMP-9, the inflammatory disorder patient is identified as a patient who responds to therapy.

50. The method of claim 39, wherein when the patient has a first concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 greater than healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9 less than healthy volunteer average concentrations for totMMP-9, and a second concentration of IL-17A, IL-17A/F and IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β substantially the same as healthy volunteer average concentrations for IL-1 β , a concentration of IL-6 substantially the same as healthy volunteer average concentrations for IL-6, and a concentration of totMMP-9

substantially the same as healthy volunteer average concentrations for totMMP-9, the inflammatory disorder patient is identified as a patient who responds to therapy.

51. The method of claim 39, wherein when the patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, or a concentration of totMMP-9 greater than about 5.0 ng/ml, the inflammatory disorder patient is identified as a patient who responds to therapy.

52. The method of claim 39, wherein when the patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with one or more of a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, or a concentration of totMMP-9 greater than about 5.0 ng/ml, the inflammatory disorder patient is identified as a patient who responds to therapy.

53. The method of claim 39, wherein when the patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml or of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml or of IL-17F of less than about 116 pg/ml, in combination with a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater

than about 5.0 ng/ml, the inflammatory disorder patient is identified as a patient who responds to therapy.

54. The method of claim 39, wherein when the patient has a first concentration of IL-17A greater than about 0.18 pg/ml, of IL-17A/F greater than about 1.35 pg/ml and of IL-17F of greater than about 116 pg/ml, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A less than about 0.18 pg/ml, of IL-17A/F less than about 1.35 pg/ml and of IL-17F of less than about 116 pg/ml, in combination with a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the inflammatory disorder patient is identified as a patient who responds to therapy.

55. The method of claim 39, wherein when the patient has a first concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A, IL-17A/F or IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F or IL-17F, in combination with one or more of a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the inflammatory disorder patient is identified as a patient who responds to therapy.

56. The method of claim 39, wherein when the patient has a first concentration of IL-17A, IL-17A/F or IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A, IL-17A/F or IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F or IL-17F, in combination with a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of

IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the inflammatory disorder patient is identified as a patient who responds to therapy.

57. The method of claim 39, wherein when the patient has a first concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, or a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A, IL-17A/F and IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F and IL-17F, in combination with one or more of a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the inflammatory disorder patient is identified as a patient who responds to therapy.

58. The method of claim 39, wherein when the patient has a first concentration of IL-17A, IL-17A/F and IL-17F greater than healthy volunteer average concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β less than about 1.1 pg/ml, a concentration of IL-6 greater than about 1.0 pg/ml, and a concentration of totMMP-9 less than about 5.0 ng/ml, and a second concentration of IL-17A, IL-17A/F and IL-17F substantially the same as healthy volunteer concentrations for IL-17A, IL-17A/F and IL-17F, in combination with a concentration of IL-1 β greater than about 1.1 pg/ml, a concentration of IL-6 less than about 1.0 pg/ml, and a concentration of totMMP-9 greater than about 5.0 ng/ml, the inflammatory disorder patient is identified as a patient who responds to therapy.

59. The method of any of claims 1-58, wherein the inflammatory disorder is selected from the group consisting of RA, Crohn's Disease, IBD, ulcerative colitis, psoriasis, or COPD.

60. The method of claim 59, wherein the inflammatory disorder is RA.

61. The method of claim 59, wherein the inflammatory disorder is Crohn's Disease.

62. The method of claim 59, wherein the inflammatory disorder is IBD.

63. The method of claim 59, wherein the inflammatory disorder is ulcerative colitis.
64. The method of claim 59, wherein the inflammatory disorder is psoriasis.
65. The method of claim 59, wherein the inflammatory disorder is COPD.
66. A method for predicting the rate of inflammatory disease progression in a subject, comprising:
- (a) obtaining a sample from the subject;
 - (b) determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample;
- wherein when the concentration of none or one of IL-17A is greater than 0.18 pg/ml, IL-17-F is greater than 116 pg/ml, or IL-17A/F is greater than 1.35 pg/ml,
- and wherein when the concentration of one of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, or IL-6 is greater than 1.0 pg/ml,
- the subject is predicted to have a slow rate of inflammatory disease progression.
67. The method of claim 66, wherein when the concentrations of one of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, and the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of one or more of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a medium rate of inflammatory disease progression.
68. The method of claim 66, wherein when the concentrations of one or more of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, and the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of at least two of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a high rate of inflammatory disease progression.

69. A method for predicting the likelihood of inflammatory disease remission in a subject, comprising:

- (a) obtaining a sample from the subject;
- (b) determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample;

wherein when the concentration of none or one of IL-17A is greater than 0.18 pg/ml, IL-17-F is greater than 116 pg/ml, or IL-17A/F is greater than 1.35 pg/ml,

and wherein when the concentration of one of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, or IL-6 is greater than 1.0 pg/ml,

the subject is predicted to have a high likelihood of inflammatory disease remission.

70. The method of claim 69, wherein when the concentrations of one of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, and the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of one or more of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a medium likelihood of inflammatory disease remission.

71. The method of claim 69, wherein when the concentrations of one or more of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, and the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of at least two of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is predicted to have a low likelihood of inflammatory disease remission.

72. A method for determining the severity of inflammatory disease in a subject, comprising:

- (a) obtaining a sample from the subject;
- (b) determining a concentration of each of IL-17A, IL-17A/F, and IL-17F, and optionally one or more of IL-1 β , IL-6, totMMP-9, proMMP-9, cTnI, and combinations thereof in the sample;

wherein when the concentration of one of IL-17A is greater than 0.18 pg/ml, IL-17-F is greater than 116 pg/ml, or IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of none or one of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, or IL-6 is greater than 1.0 pg/ml, the subject is determined to have mild inflammatory disease.

73. The method of claim 72, wherein when the concentrations of at least one of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, or the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of one or more of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is determined to have moderate inflammatory disease.

74. The method of claim 72, wherein when the concentrations of at least one of IL-17A is greater than 0.18 pg/ml, the concentration of IL-17-F is greater than 116 pg/ml, and the concentration of IL-17A/F is greater than 1.35 pg/ml, and wherein when the concentration of two or more of IL-1 β is less than 1.1. pg/ml, totMMP-9 is less than 5.0 ng/ml, and IL-6 is greater than 1.0 pg/ml, the subject is determined to have severe inflammatory disease.

75. The method of any of claims 66-74, wherein the inflammatory disease is selected from the group consisting of RA, Crohn's Disease, IBD, ulcerative colitis, psoriasis, or COPD.

76. The method of claim 75, wherein the inflammatory disease is RA.

77. The method of claim 75, wherein the inflammatory disease is Crohn's Disease.

78. The method of claim 75, wherein the inflammatory disease is IBD.

79. The method of claim 75, wherein the inflammatory disease is ulcerative colitis.

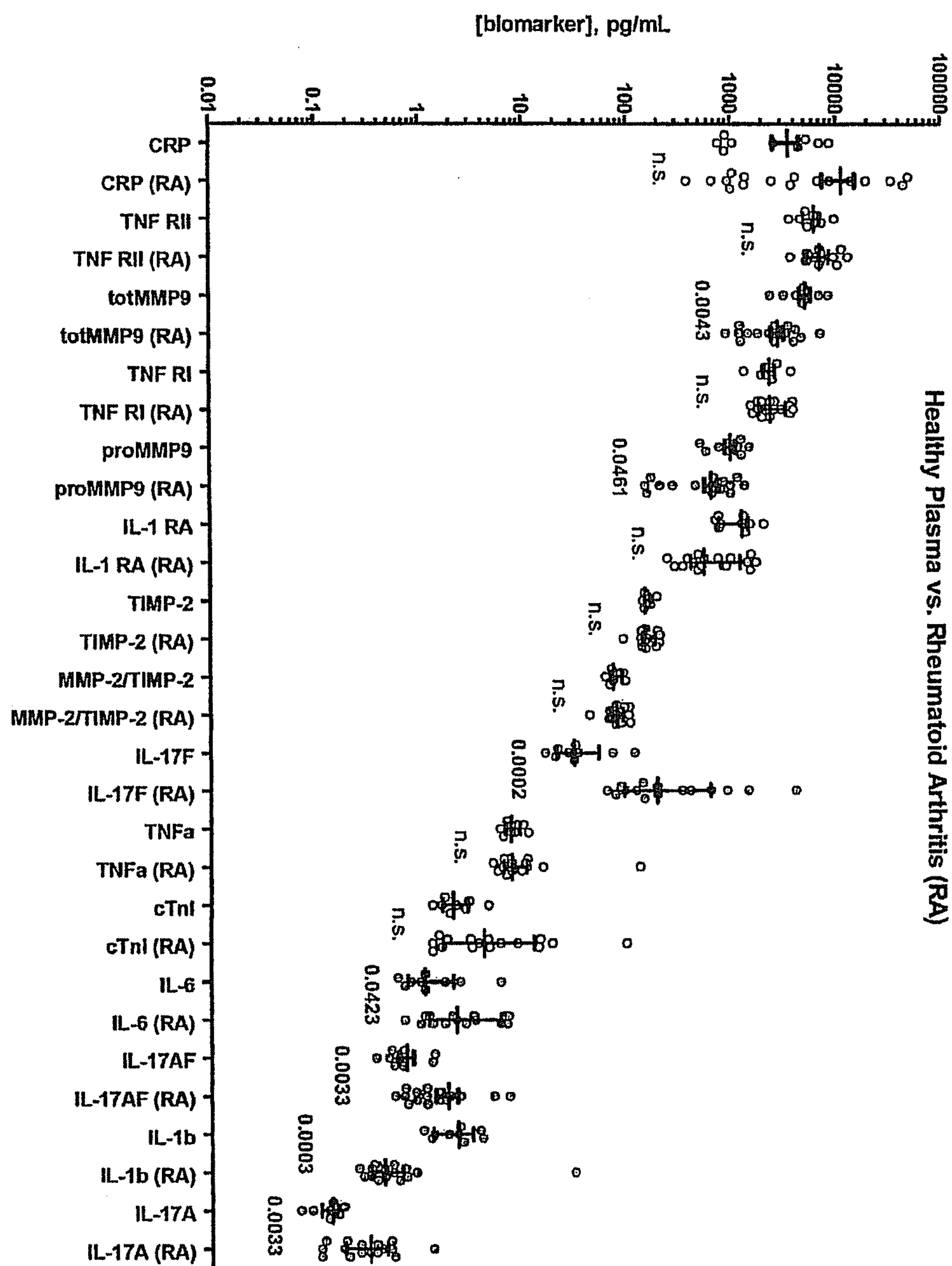
80. The method of claim 75, wherein the inflammatory disease is psoriasis.

81. The method of claim 75, wherein the inflammatory disease is COPD.

82. A method for determining inflammatory disease in a patient comprising
- (a) detecting the concentration of more or more the following markers in a patient sample: IL-17A, IL-17F, IL-17A/F, IL-1 β , IL-6, totMMP-9, proMMP-9, and cTnI;
 - (b) comparing the level of the one or more markers to the level in a normal population of healthy volunteers; and
 - (c) determining that the patient has inflammatory disease when the concentration of IL-17A, IL-17F, IL-17A/F, IL-6, or cTnI are elevated relative to the normal population, or totMMP-9, proMMP-9, or IL-1 β are decreased relative to the normal population.
83. The method of claim 82, wherein the disease is RA and the one or more markers comprises the combination of IL-17F & IL-17A, the combination of IL-17A and IL-17 A/F, or the combination of IL-17F and IL-17 A/F.

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FIG. 1



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FIG 2A

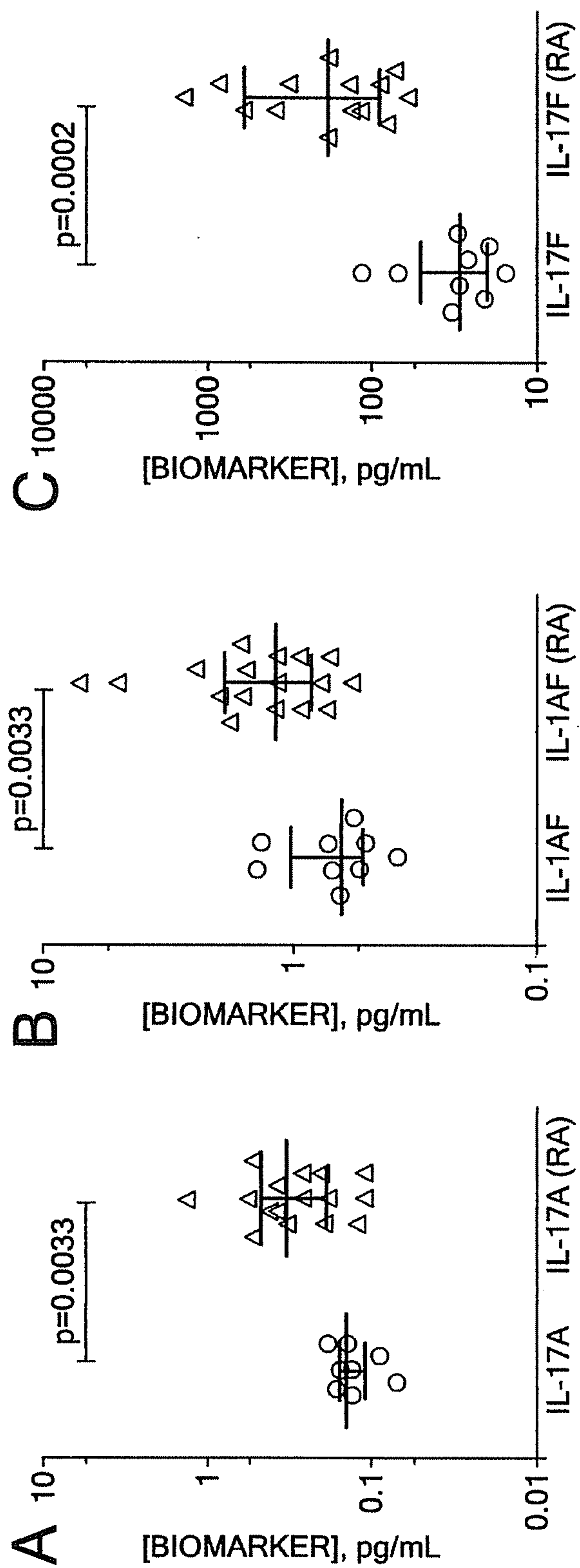


FIG. 2B

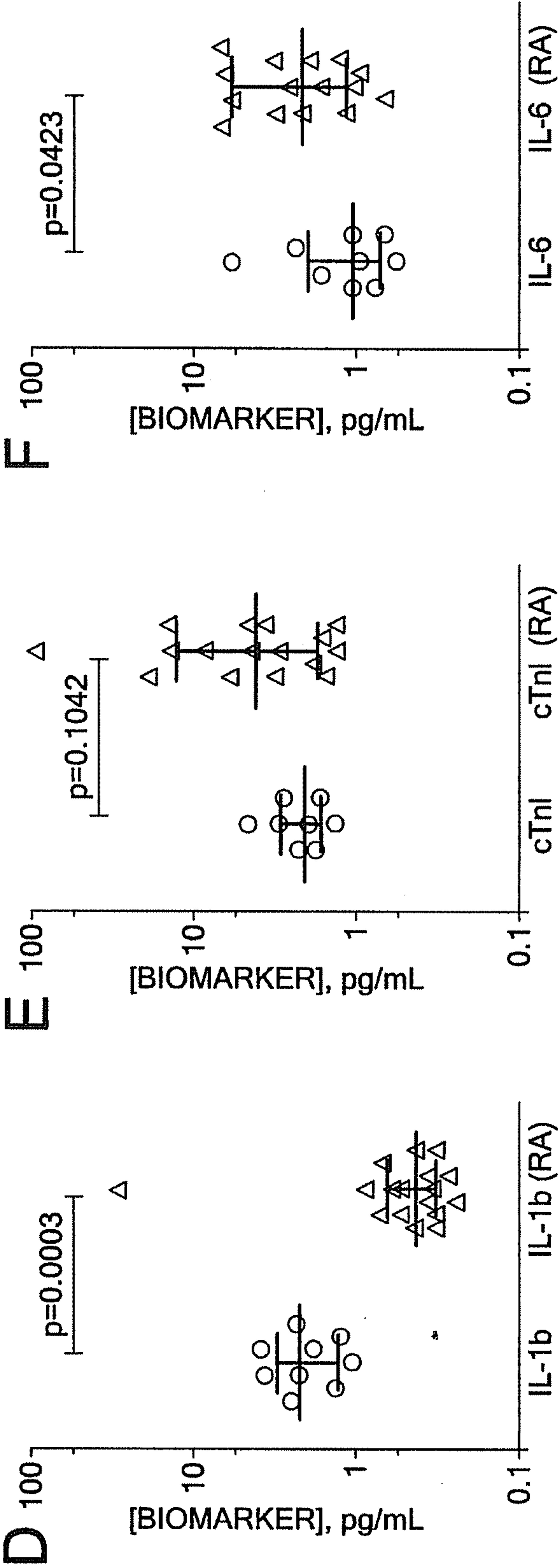
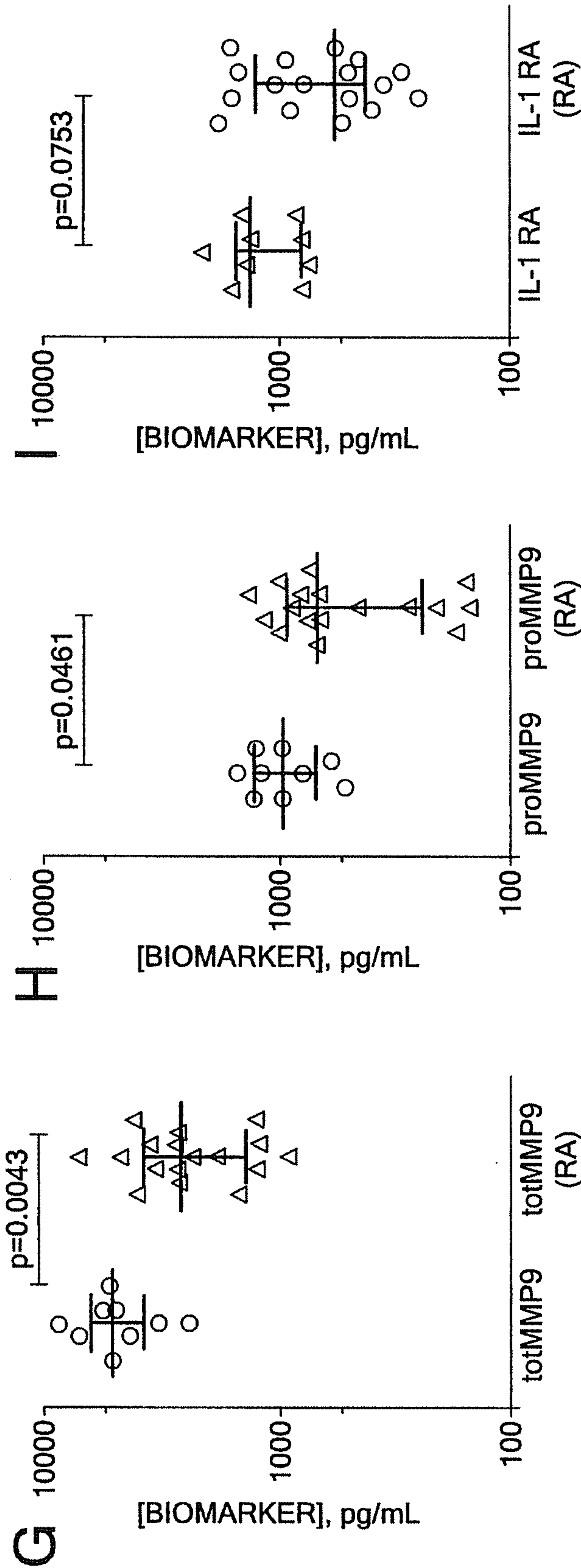


FIG. 2C



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FIG. 3

Synergy between IL-17 biomarkers

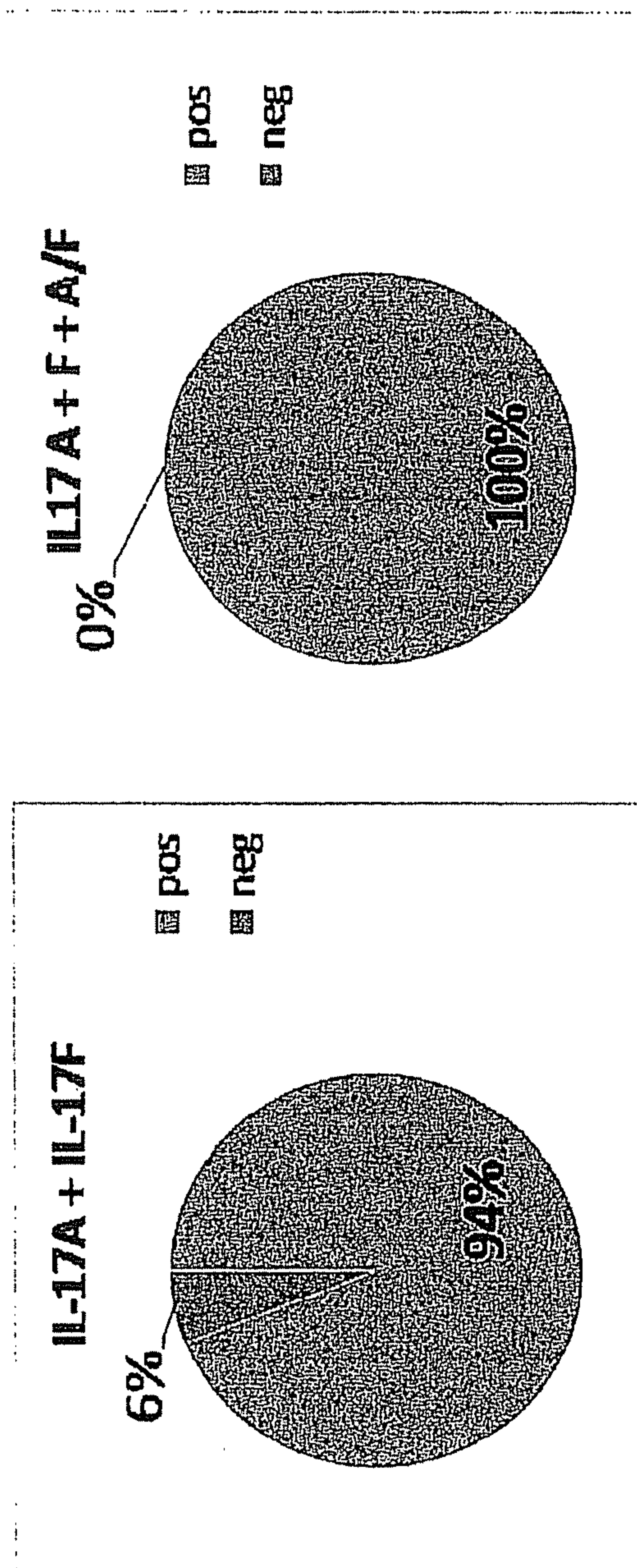


FIG. 4A

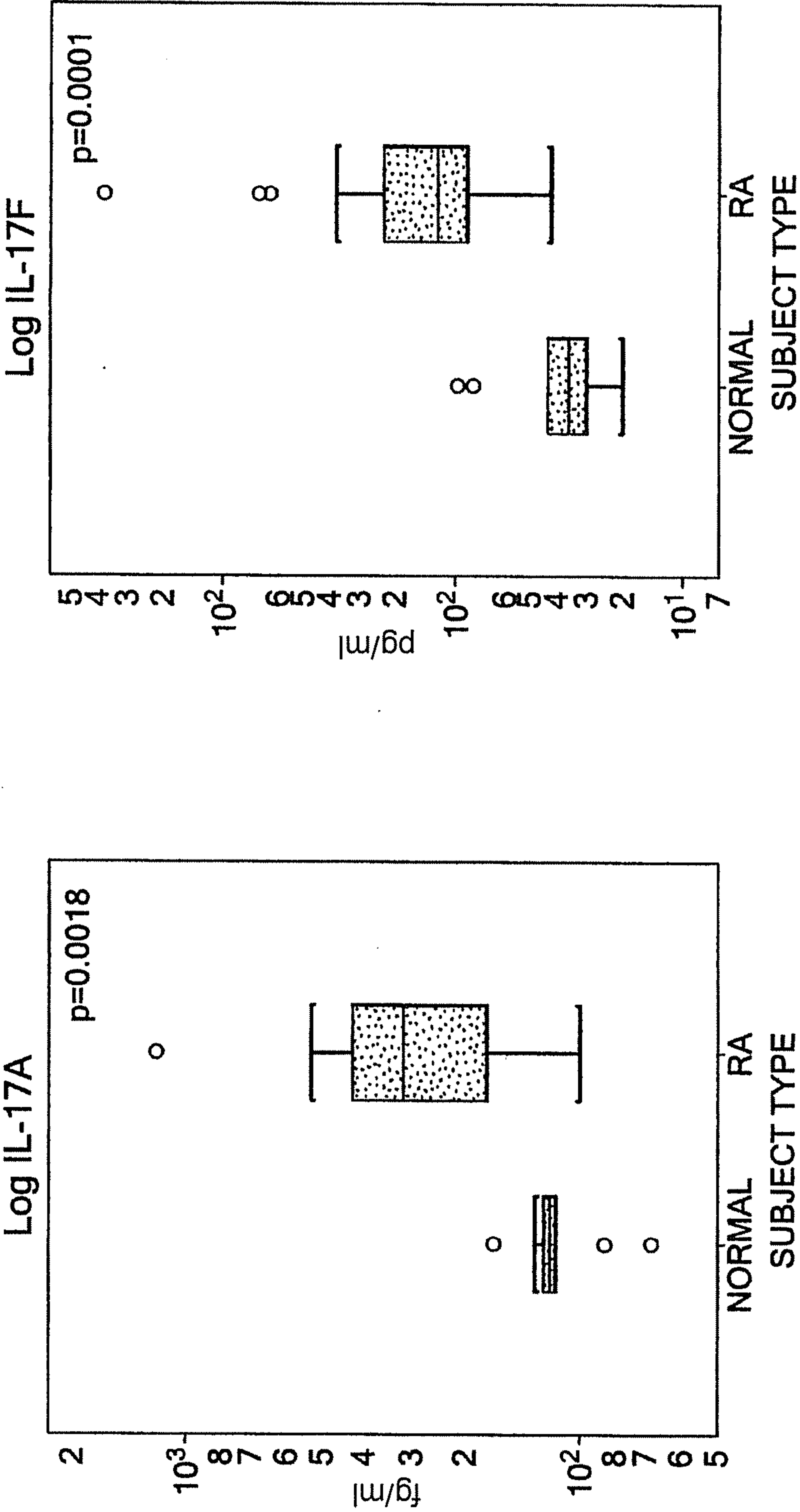


FIG. 4B

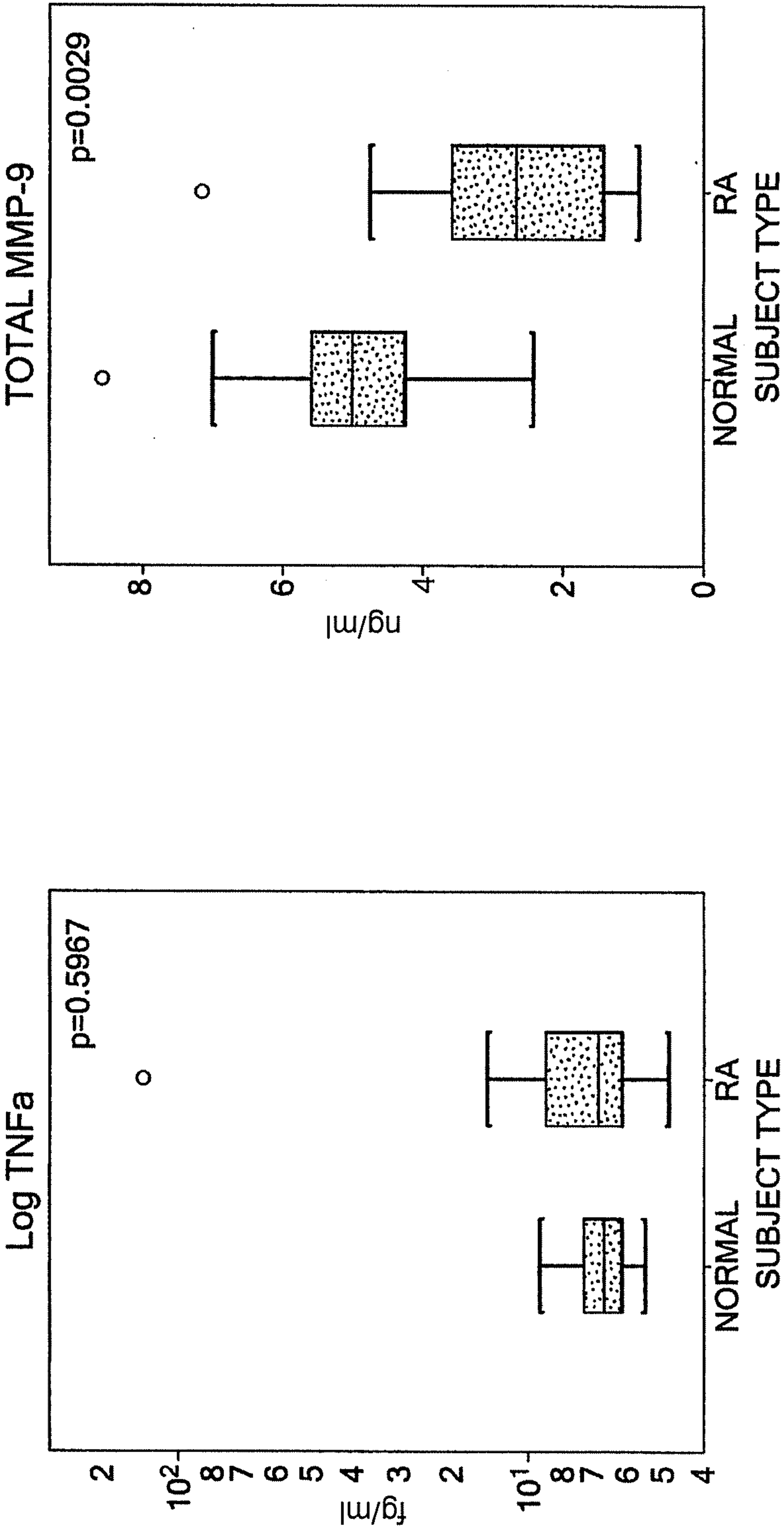
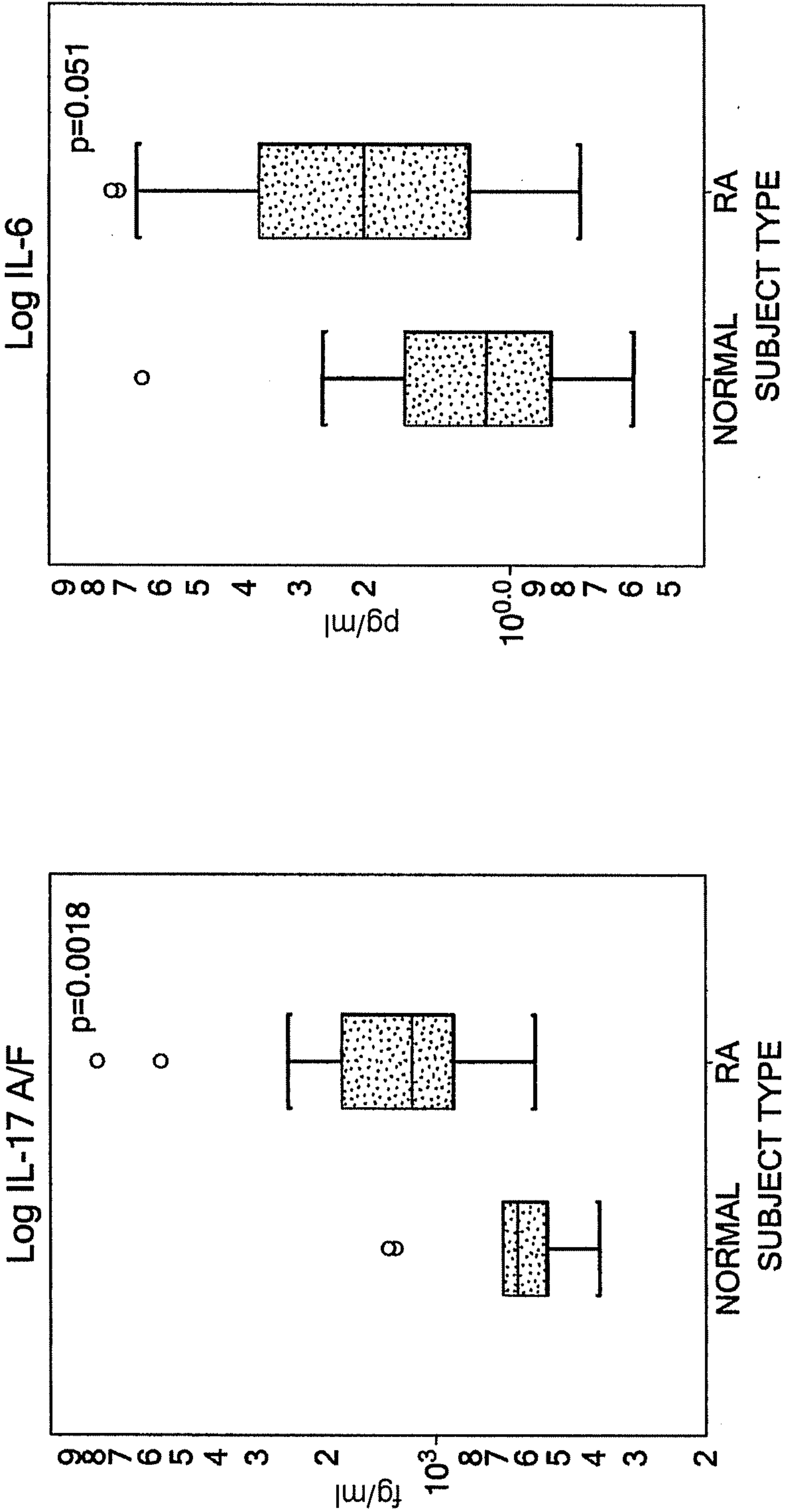
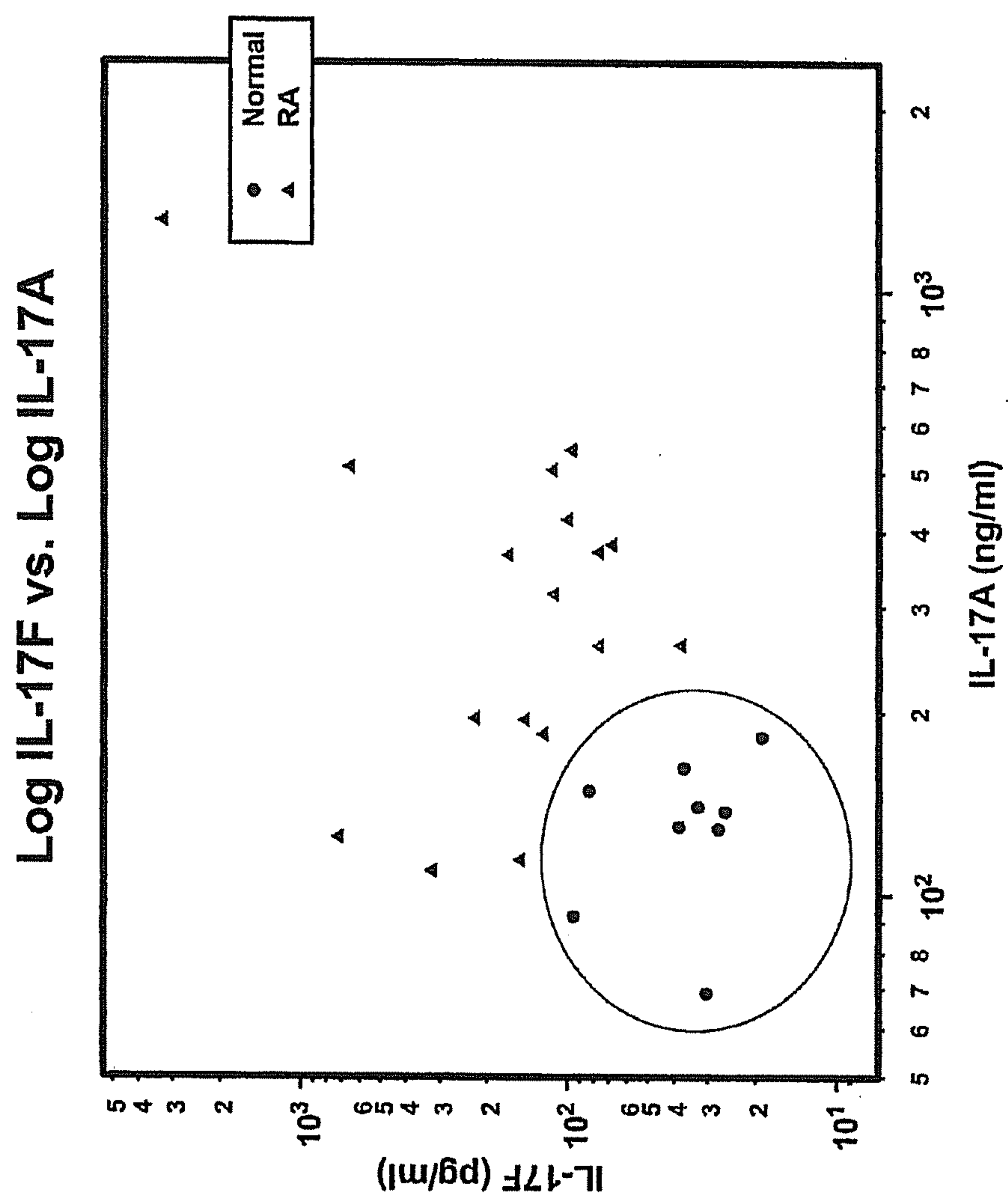


FIG. 4C

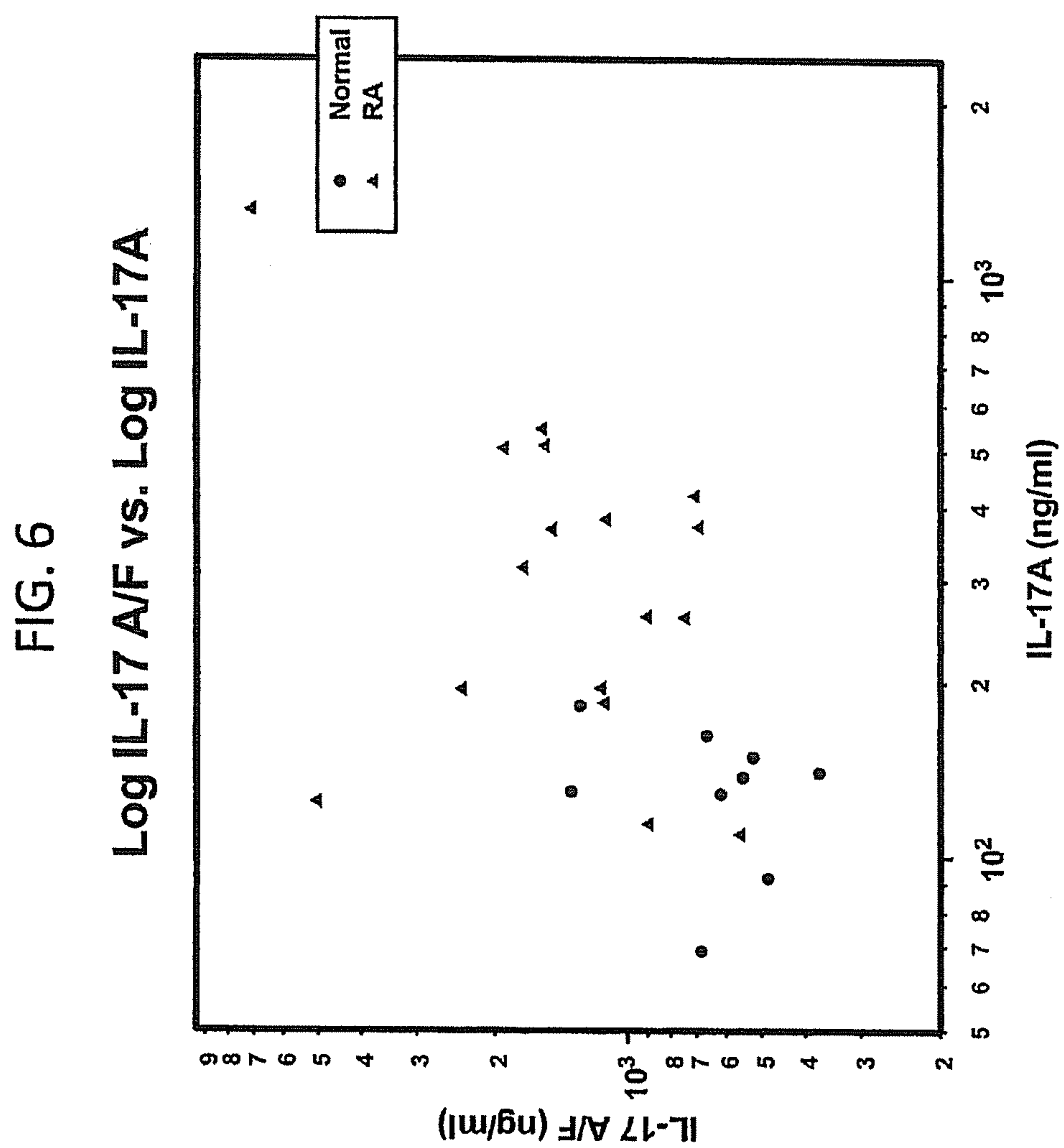


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FIG. 5



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