Claims

1. A method for predicting a response to adalimumab from a serum/plasma sample extracted from a rheumatoid arthritis patient prior to treating the patient with adalimumab, said response being classified as a good response corresponding to anti-drug antibody negative or a poor response corresponding to anti-drug antibody positive, comprising the steps of:

   (i) testing the sample for the presence of autoantibody biomarkers; and

   (ii) determining whether the patient will develop a good response or a poor response to treatment with adalimumab, based on the detection of said autoantibody biomarkers;

   characterised in that said autoantibody biomarkers comprise autoantibodies to antigens SSB, TROVE2 and ZHX2, wherein ZHX2 is associated with the good response, and SSB and TROVE2 are associated with the poor response.

2. The method according to claim 1 wherein the autoantibody biomarkers further comprise autoantibodies to one or more antigens from the group comprising of: PPARD, TRIB2, SH3GL1, ODC1, EEF1D, PRKAR1A and EAPP which are associated with the good response, and SPANXN2, HNRNPA2B, CEP55, FN3K, PANK3, HPCAL1, THRA, AIFM1, RPS6KA4, KLF10 and EPHA2 which are associated with the poor response.

3. The method according to claim 1 or 2 wherein the antigens are biotinylated proteins.

4. The method according to claim 3 wherein each biotinylated protein is formed from a Biotin Carboxyl Carrier Protein folding marker which is fused in-frame with a protein.

5. The method according to claim 3 or 4 wherein the biotinylated proteins are bound to a streptavidin-coated substrate.

6. The method according to claim 5 wherein the substrate comprises a hydrogel-forming polymer base layer.

7. The method according to any preceding claim wherein the antigens are exposed to a serum/plasma sample extracted from a rheumatoid arthritis patient, such that autoantibody biomarkers from the sample may bind to the antigens.

8. The method according to claim 7 wherein the antigens are subsequently exposed to a fluorescently-tagged secondary antibody to allow the amount of any autoantibodies from the sample bound to the antigens to be determined.

9. The method according to claim 8 wherein the patient's response to treatment with adalimumab corresponds to the relative or absolute amount of autoantibodies from the sample specifically binding to the antigens.

10. The method according to any preceding claim wherein the steps are performed *in vitro*.

11. The method according to any preceding claim wherein the method comprises detecting upregulation/downregulation of one or more biomarkers.

12. A method for manufacturing a kit which is used to predict a response to adalimumab from a serum/plasma sample extracted from a rheumatoid arthritis patient prior to treating the patient with adalimumab, said response being classified as a good response corresponding to anti-drug antibody negative or a poor response corresponding to anti-drug antibody positive, comprising the steps of:

for each antigen in a panel, cloning a biotin carboxyl carrier protein folding marker in-frame with a gene encoding the antigen and expressing the resulting biotinylated antigen;

binding the biotinylated antigens to addressable locations on one or more streptavidin-coated substrates, thereby forming an antigen array;

such that the amount of autoantibodies from the sample binding to the antigens on the panel can be determined by exposing the substrate to the sample and measuring the response;

characterised in that the antigens comprise SSB, TROVE2 and ZHX2, wherein ZHX2 is associated with the good response, and SSB and TROVE2 are associated with the poor response.

13. The method according to claim 12 wherein the antigens further comprise one or more of: PPARD, TRIB2, SH3GL1, ODC1, EEF1D, PRKAR1A and EAPP which are associated with the good response, and SPANXN2, HNRNPA2B, CEP55, FN3K, PANK3, HPCAL1, THRA, AIFM1, RPS6KA4, KLF10 and EPHA2 which are associated with the poor response.

14. A composition comprising a panel of antigens which is used to predict an immunogenic and/or therapeutic response to adalimumab in a rheumatoid arthritis patient who has not previously been treated with adalimumab, said response being classified as a good response corresponding to anti-drug antibody negative or a poor response corresponding to anti-drug antibody positive, characterised in that the antigens comprise SSB, TROVE2 and ZHX2, wherein ZHX2 is associated with the good response, and SSB and TROVE2 are associated with the poor response.

15. A composition according to claim 14 wherein the antigens further comprise one or more of PPARD, TRIB2, SH3GL1, ODC1, EEF1D, PRKAR1A and EAPP which are associated with the good response, and SPANXN2, HNRNPA2B, CEP55, FN3K, PANK3, HPCAL1, THRA, AIFM1, RPS6KA4, KLF10 and EPHA2 and which are associated with the poor response.

16. A composition according to claim 14 or 15 wherein the antigens are biotinylated proteins.

17. A composition according to any of claims 14-16 wherein the amount of one or more autoantibody biomarkers binding *in vitro* to the antigens in a sample from a patient can be measured to predict the response.

18. A composition comprising a panel of autoantibody biomarkers which is used to predict an immunogenic and/or therapeutic response to adalimumab in a rheumatoid arthritis patient who has not previously been treated with adalimumab, said response being classified as a good response corresponding to anti-drug antibody negative or a poor response corresponding to anti-drug antibody positive,

wherein the level of the autoantibody biomarkers are measured in a serum/plasma sample collected from the patient;

characterised in that the autoantibody biomarkers are specific to antigens comprising SSB, TROVE2 and ZHX2, wherein ZHX2 is associated with the good response, and SSB and TROVE2 are associated with the poor response.