WHAT IS CLAIMED IS:

1. ~~A~~An *in vitro* method for monitoring and predicting a rheumatoid arthritis (RA) flare or increased RA disease activity in a patient comprising:

(a) isolating a blood sample from said patient;

(b) evaluating the blood sample for expression or quantitatively increased amounts of one or more sets of antecedent RNA markers, protein markers or cell markers selected from:

(i) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;

(ii) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;

(iii) AC2 markers or proteins as provided in Table 7;

(iv) AC3 markers or proteins as provided in Table 8; and

(v) cell markers CD45- CD31-PDPN+;

(c) wherein the expression or quantitatively increased amounts of the RNA markers or proteins or the presence of the cell markers predicts an impending RA flare.

2. The method of claim 1, wherein the expression or quantitatively increased amounts of the AC2 RNA markers or proteins predicts an RA flare in about 2 weeks or about 12-14 days or up to 3 weeks~~.~~ and/or the expression or quantitatively increased amounts of the AC3 RNA markers or proteins predicts an RA flare in about 1 week or about 5-7 days or up to 2 weeks.

~~3. The method of claim 1, wherein the expression or quantitatively increased amounts of the AC3 RNA markers or proteins predicts an RA flare in about 1 week or about 5-7 days or up to 2 weeks.~~

~~4.~~3. The method of claim 1, wherein a subset of at least 20 of the AC2 or AC3 markers are evaluated.

~~5. The method of claim 1, wherein a subset of at least 20 of the AC2 and at least 20 of the AC3 markers are evaluated.~~

~~6.~~4. The method of claim 1, wherein a subset of at least 10 of the AC2 or AC3 markers are evaluated.

~~7. The method of claim 1, wherein a subset of at least 10 of the AC2 and at least 10 of the AC3 markers are evaluated.~~

~~8.~~5. The method of claim 1, wherein sublining fibroblast markers selected from the AC3 markers or proteins are evaluated.

~~9.~~6. The method of claim 1, wherein AC3 markers or proteins expressed by CD34+, HLADR+ and DKK3+ cells are evaluated.

~~10.~~7. The method of claim 1, wherein the cell marker IL17RD is also evaluated.

~~11.~~8. The method of claim 1, wherein RNA expression is assessed by RT PCR, protein expression is assessed using specific antibodies, and cell markers are evaluated using FACs analysis.

~~12. The method of claim 1 wherein protein expression is assessed using specific antibodies.~~

~~13. The method of claim 1 wherein cell markers are evaluated using FACs analysis.~~

~~14.~~9. The method of claim 1 wherein the antecedent RNA markers or protein markers or selected from:

(a) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;

(b) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9; and

(c) AC3 markers or proteins as provided in Table 8;

are reduced, significantly decreased, nearly absent, or absent in peripheral blood during an RA flare or once a patient exhibits symptoms of an RA flare.

~~15.~~10. ~~A~~An *in vitro* method for predicting an impending RA flare and treating a flare in a patient, the method comprising:

a) isolating a blood sample from the patient;

b) contacting the blood sample with reagents specific for markers selected from a panel of RNA or protein markers to assess expression of the RNA or protein markers, wherein the panel of RNA or protein markers is selected from:

(i) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;

(ii) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;

(iii) AC2 markers or proteins as provided in Table 7; and

(iv) AC3 markers or proteins as provided in Table 8;

c) comparing expression of the markers selected from a panel of RNA or protein markers in the blood sample to expression of the markers in a control blood sample to determine if expression of the markers selected from a panel of RNA or protein markers in the blood sample is increased relative to expression in the control blood sample, wherein detection of increased expression serves to predict an impending RA flare in a patient;

and treating the patient thereby diagnosed with an impending RA flare by administering a therapeutically effective amount of one or more disease modifying agent for treating RA.

~~16. The method of claim 15, wherein RNA expression is assessed by RT PCR.~~

~~17. The method of claim 15, wherein protein expression is assessed using specific antibodies.~~

~~18.~~11. The method of claim ~~15~~ 10, wherein the expression or quantitatively increased amounts of the AC2 RNA markers or proteins predicts an RA flare in about 2 weeks or about 12-14 days or about 3 weeks.

~~19.~~12. The method of claim ~~15~~ 10, wherein the expression or quantitatively increased amounts of RNA or protein markers selected from:

(a) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6;

(b) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4; and

(c) the AC3 RNA markers or proteins;

predicts an RA flare in about 1 week or about 5-7 days or about 2 weeks.

~~20.~~13. The method of claim ~~15~~ 10, wherein the disease modifying agent for treating RA is one or more agent selected from a nonsteroidal anti-inflammatory drug (NSAID), steroid, methotrexate,

disease-modifying antirheumatic drug (DMARDs), biologic DMARD, and oral janus kinase (JAK) inhibitor.

~~21. The method of claim 20, wherein the DMARD is selected from methotrexate (Trexall, Otrexup), leflunomide (Arava), hydroxychloroquine (Plaquenil) and sulfasalazine (Azulfidine).~~

~~22. The method of claim 20, wherein the biologic DMARD is selected from abatacept (Orencia), adalimumab (Humira), anakinra (Kineret), baricitinib (Olumiant), certolizumab (Cimzia), etanercept (Enbrel), golimumab (Simponi), infliximab (Remicade), rituximab (Rituxan), sarilumab (Kevzara), tocilizumab (Actemra) and tofacitinib (Xeljanz).~~

~~23. The method of claim 20, wherein the biologic DMARD is a tumor necrosis factor (TNF) inhibitor.~~

~~24. The method of claim 20, wherein the biologic DMARD is combined with an NSAID and/or with methotrexate.~~

~~25. The method of claim 20, wherein the JAK inhibitor is selected from tofacitinib (Xeljanz and Xeljanz XR), baricitinib (Olumiant), and upadacitinib (Rinvoq).~~

~~26.~~14. The method of claim ~~15~~ 10, wherein the disease modifying agent for treating RA is an IL-17 antibody or an IL17RD blocking antibody.

~~27.~~15. A circulating pre-inflammatory mesenchymal (PRIME) cell characterized as a CD45-CD31-PDPN+ cell, wherein the presence of the cell in peripheral blood is indicative or predictive of an impending RA flare.

~~28.~~16. The PRIME cell of claim ~~27~~ 15, which additionally expresses IL17RD and is IL17RD+.

~~29.~~17. ~~A~~An *in vitro* method of predicting an impending RA flare comprising evaluating a blood sample from a patient for the presence of a PRIME cell characterized as a CD45-CD31-PDPN+ cell, wherein the presence of detectable PRIME cells in peripheral blood in a patient predicts an impending RA flare in the patient.

~~30.~~18. The method of claim ~~29~~ 17, further evaluating for the presence of IL17RD on a CD45-CD31-PDPN+ cell.

~~31.~~19. ~~A~~An *in vitro* method for evaluating and treating an impending flare in an RA patient comprising evaluating the peripheral blood of a patient for the presence of a PRIME cell characterized as a CD45-CD31-PDPN+IL17RD+ cell and treating a patient that is positive for PRIME cells in their peripheral blood with a disease modifying agent for RA.

~~32.~~20. The method of claim ~~31~~ 19, wherein the patient is treated with an IL-17 or IL-17RD antibody.

~~33. The method of claim 32, wherein the patient is further treated with an anti-inflammatory agent and/or an immune modulating agent.~~

~~34.~~21. A set of RNA or protein markers for evaluating and predicting an impending RA flare in a patient comprising the markers selected from:

(i) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;

(ii) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;

(iii) a subset of at least 20 markers from the AC2 markers provided in Table 7; and

(iv) a subset of at least 20 markers from the AC3 markers provided in Table 8.

~~35.~~22. The marker set of claim ~~34~~ 21, wherein the subset of AC2 markers comprises naïve B cell gene markers and markers of developmental pathways for naïve B cells and leukocytes~~,~~ and the subset of AC3 markers comprises markers of cartilage morphogenesis, endochondral bone growth, extracellular matrix organization and sublining fibroblasts.

~~36. The marker set of claim 34, wherein the subset of AC3 markers comprises markers of cartilage morphogenesis, endochondral bone growth, extracellular matrix organization and sublining fibroblasts.~~

~~37.~~23. A system or kit for predicting an impending RA flare comprising a set of markers of claim ~~34~~ 21 or a set of probes and/or antibodies for evaluating a set of markers of claim ~~34~~ 21.

~~38.~~24. The system or kit of claim ~~37~~ 23, which further comprises a means for collection of the patient's blood by fingerstick.