**Supplementary Table 1**

Cohort 1: Newly diagnosed RA and healthy controls.

|                          | Cohort 1 ERA (n=14) | Cohort 1 HD (n=16) |
|--------------------------|----------------------|---------------------|
| Age (year, IQR)          | 52.6 (36.66;5.5)    | 53.1 (43.5;60.3)    |
| Female (number)          | 11 (78.6%)          | 10 (62.5%)          |
| CCP (IU/ml, IQR)         | 290.8 (94;503.3)    | N/A                 |
| RF (IU/ml, IQR) *1       | 86.4 (15.9;67.9)    | N/A                 |
| Baseline DAS28 (IQR) *2  | 5.4 (4.8;6.4)       | N/A                 |
| Follow up DAS28 at 6 months (IQR) *3 | 4.1 (2.8;5.6) | N/A |

*1n=9, *2n=10, *3n=9

**Supplementary Table 2**

Cohort 2: Scottish Early Arthritis (SERA) study

(i) Baseline data

|                          | SERA study (n=113) |
|--------------------------|---------------------|
| Age (year, IQR)          | 61.9 (53.6;71.1)    |
| Female (number)          | 65 (57.5%)          |
| CCP (IU/ml, IQR) *1      | 210.2 (5.7;340)     |
| RF (IU/ml, IQR) *2       | 175.2 (15;348.5)    |
| Baseline DAS28 (IQR)     | 5.0 (3.8;6.1)       |
| Follow up DAS28 at 6 months (IQR) | 3.8 (2.3;5.3) | |

*1n=97, *2n=64

(ii) SERA: 6 months post DMARD treatment

|                          | SERA study (n=12) |
|--------------------------|-------------------|
| Age (year, IQR)          | 64.6 (54.9;79.7)  |
| Female (number)          | 8 (66.7%)         |
| CCP (IU/ml, IQR)         | 186.9 (39.340)    |
| RF (IU/ml, IQR) *1       | 231 (20;501)      |
| Baseline DAS28 (IQR)     | 5.1 (3.6;6.4)     |
| 6 month DAS28 (IQR)      | 4.9 (3.3;6.7)     |
| DMARD treatment          |                   |
| - Methotrexate           | 10                |
| - Hydroxychloroquine     | 4                 |
| - Sulfasalazine          | 5                 |
| - Leflunomide            | 1                 |
| Number of concurrent DMARDS |          |
| - One                    | 7                 |
| - Two                    | 2                 |
| - Three                  | 3                 |

*1n=3
Supplementary Table 3A  
Cohort 3: Patients with established RA that had failed synthetic DMARD therapy

| Age (years, IQR) | 52.6 (37;67.8) |
| Gender (female) | 12 (75%) |
| CCP (IU/ml, IQR) | 232.1 (61.8;405) |
| RF (IU/ml, IQR) | 69.3 (10.6;131) |
| DMARD (current/previous failed) |   |
| - Methotrexate | 16 |
| - Hydroxychloroquine | 12 |
| - Sulfasalazine | 15 |
| - Leflunomide | 10 |
| - Gold | 2 |
| - Cyclosporin | 1 |
| Number of previous Biologic DMARDs |   |
| - None | 1 |
| - One | 6 |
| - Two | 6 |
| - Three | 2 |
| - Four | 1 |
| Biologic agents (current/previous failed) |   |
| - Certolizumab | 14 |
| - Etanercept | 6 |
| - Adalimumab | 1 |
| - Rituximab | 4 |
| - Tocilizumab | 2 |
| - Abatacept | 1 |

*N=14, *2N=11

Supplementary Table 3B

| Sjogren's Syndrome patients | (n=14) |
| Age (year, IQR) | 50.5 (38;64) |
| Female [number (n)] | 12 (87%) |
| Positive for either anti Ro/La | 100% |
| RF (IU/ml, IQR) n=12 patients | 83 (2.7;290) |
| Anti-dsDNA (IU/ml) n=1 patient | 38.7 |

Supplementary Table 3C

| Age (year, IQR) | RA cohort for fig 4B Baseline (n=39) 6m (n=38) | RA cohort for fig 4C Baseline and 6m (n=27) |
| Female (number) | 25 (64.1%) | 17 (63%) |
| CCP (IU/ml, IQR) | 154.1 (6.4;340) *1 | 112.7 (5.3;288) *4 |
| RF (IU/ml, IQR) | 214.3 (20;277) *2 | 229.3 (20;442) *5 |
| Baseline DAS28 (IQR) | 5.0 (3.8;5.9) | 5.0 (4.1;5.9) |
| DAS28 at 6 months (IQR) | 3.9 (2.7;4.9) *3 | 3.9 (2.3;5.3)*6 |

*n=30, *2n=31, *3n=35, *4n=19, *5n=23, *6n=24,
Supplementary Table 4

Cohort 4: Matched synovial and peripheral blood samples from joint arthroplasty

| Sex          | 6 Female, 2 Male |
|--------------|-----------------|
| Serum CCP and RF | 8/8 CCP positive, 6/6 RA positive (data not available for 2 samples) |
| Smoking      | 4/5 smokers (data not available for 3 samples) |
| Synovial sampling site | 7 knee, 1 hip |
| DMARD therapy at time of sampling | Sulphasalazine 1, Tocilizumab 1, NIL 1, Prednisolone 1, Sulphasalazine/Methotrexate 2, Prednisolone/Azathioprine 1, Methotrexate/Humira 1 |

Supplementary Table 5

Supplementary table 5: Methods summary for cell preparation and B cell repertoire amplification

| Cohort | Description | Cell site and RNA preparation | Amplification method | Isotype(s) amplified* |
|--------|-------------|-------------------------------|----------------------|-----------------------|
| 1      | Early RA (ERA) and control donors, n=14 and n=16 | PBMC purification, CD19+MACS | PCR amplification using IGHV FR1 primers, IGHC primers | IgM & IgG |
| 2      | Early RA (ERA), n=113 | Paxgene tubes – 3 mL whole blood. | PCR amplification using IGHV FR1 primers, IGHC primers | IgG |
| 3      | Established RA (ESRA), n=16 | PBMC purification, CD19+MACS | PCR amplification using IGHV FR1 primers, IGHC primers | IgG |
| 4      | Paired PBMC and synovial B cells and CD27 sorted B cells | CD20+, IgG+, CD27+or CD27- | SMARTseq2 whole-transcriptome amplification followed by PCR amplification using IGHV FR1 primers, IGHC primers | IgG |

*for primer information, see supplementary figure 1
### Supplementary Table 6: Antibody reagents for flow cytometry

| Antibody Reagent                  | Clone Reference |
|-----------------------------------|-----------------|
| CD19-PE/Cy5                       | HIB19           |
| CD20-APC                          | 2H7             |
| CD21-BV421                        | B-ly4           |
| CD27-APC                          | M1271           |
| CD38-BV510                        | HIT2            |
| CD73-BV605                        | AD2             |
| CXCR3-PE                          | IO8             |
| GMCSF-PE/CF594                    | BV2-21C11       |
| CD5-PE/Cy7                        | L17F12          |
| CD11C-BV711                       | 39              |
| CD21-PE/Cy7                       | Bu32            |
| CD21-PerCP/Cy5.5                  | Bu32            |
| CD24-BV711                        | ML5             |
| CD24-FITC                         | ML5             |
| CD38-BV605                        | HIT2            |
| CD40-APC/Cy7                      | 5C3             |
| CD86-BV711                        | IT2.2           |
| CD95(FAS)-BV510                   | DX2             |
| CD254(RANKL)-PE                   | M1H24           |
| HLA-DR-APC/Cy7                    | L243            |
| IgD-APC/Cy7                       | WA62            |
| T-Bet-PE/O7                       | 4B10            |
| TNFα-BV510                        | Mab11           |
| CD1c-PerCP/eFluor710              | L161            |
| CD20-eFluor450                    | 2H7             |
| CD307(dFcRL4)-PerCP/eFluor710     | 413D12          |
| IgG-FITC                          | IS11-3B22.3     |
| IgG-PE                            | IS11-3B22.3     |