### Supplementary Tables

**Table S1**: Summary of patient and sample data

| Patient No. | Sample No. | Tumor* | Site of biopsy | Remarks** | Lines of therapy*** |
|-------------|------------|--------|----------------|-----------|---------------------|
| 1           | 3          | t-FL   | Left axilla    | R5        | 5                   |
| 2           | 1          | FL     | Left axilla    | P         | 0                   |
| 2           | 2          | FL     | Left axilla    | P         | 5                   |
| 3           | 2          | FL     | Left inguinal biopsy | P | 2                   |
| 3           | 1          | FL     | Right axilla   | WW        | 0                   |
| 3           | 1          | FL     | Right femoral node | WW | 0                   |

*FL = Follicular lymphoma; t-FL = transformed Follicular lymphoma.
**R = relapse; P = progression; WW = no treatment received before biopsy – just watch and wait.
***Number of lines of therapy received before or between biopsies.

**Table S2 is on the next two pages.**

**Table S3**: Number of mutations from each nucleotide in tumor and non-tumor clones in each patient

| Sample       | Number of mutations from A | from C | from G | from T |
|--------------|---------------------------|--------|--------|--------|
| Pt1 tumor    | 223                       | 304    | 259    | 164    |
| Pt1 non-tumor| 209                       | 312    | 395    | 112    |
| Pt2 tumor    | 214                       | 286    | 355    | 187    |
| Pt2 non-tumor| 47                        | 121    | 164    | 62     |
| Pt3 tumor    | 297                       | 396    | 452    | 213    |
| Pt3 non-tumor| 219                       | 93     | 168    | 107    |
| FL-S         | 601                       | 765    | 917    | 348    |
| Normal GCs   | 172                       | 177    | 197    | 137    |

**Table S4**: Number of mutations from each nucleotide in tumor and non-tumor clones in each sample, in each patient

| Patient and sample | Number of mutations from A | from C | from G | from T |
|--------------------|---------------------------|--------|--------|--------|
| Pt1                | T                         | 59     | 91     | 83     | 30     |
|                    | NT                        | 115    | 159    | 233    | 41     |
| Sample 2           | T                         | 47     | 78     | 73     | 31     |
|                    | NT                        | 73     | 104    | 179    | 17     |
| Sample 1           | T                         | 77     | 132    | 110    | 49     |
|                    | NT                        | 141    | 238    | 301    | 51     |
| Pt2                | T                         | 55     | 82     | 82     | 38     |
|                    | NT                        | 36     | 92     | 116    | 35     |
| Sample 2           | T                         | 111    | 152    | 234    | 125    |
|                    | NT                        | 23     | 59     | 86     | 38     |
| Sample 1           | T                         | 95     | 154    | 134    | 55     |
|                    | NT                        | 189    | 60     | 115    | 79     |
| Pt3                | T                         | 154    | 246    | 273    | 140    |
| Sample 2           | NT                        | 45     | 36     | 61     | 33     |
### Table S2: V(D)J gene combinations detected in all clones from the FL-HTS samples

| Patient | Sample | Type | V  | D  | J  |
|---------|--------|------|----|----|----|
| Pt1     | 3 T    |      | 3-23-01 | 3-16-01 | 1-01 |
|         |        | NT   | 3-20-01 | 3-16-01 | 1-01 |
|         |        |      | 3-23-01 | 0-IR-01 | 1-01 (1) |
|         |        |      | 3-23-01 | 0-IR-01 | 1-01 (2) |
|         |        |      | 3-23-01 | 0-IR-01C | 1-01 |
|         |        |      | 3-23-01 | 0-IR-01C | 4-02 |
|         |        |      | 3-23-01 | 1-IR1-01 | 1-01 (1) |
|         |        |      | 3-23-01 | 1-IR1-01 | 1-01 (2) |
|         |        |      | 3-23-01 | 2-21-01 | 1-01 |
|         |        |      | 3-23-01 | 2-OF15-2 | 1-01 (1) |
|         |        |      | 3-23-01 | 2-OF15-2 | 1-01 (2) |
|         |        |      | 3-23-01 | 3-9-01 | 4-02 (1) |
|         |        |      | 3-23-01 | 3-9-01 | 4-02 (2) |
|         |        |      | 3-23-01 | 3-10-01 | 1-01 |
|         |        |      | 3-23-01 | 3-16-01 | 3-02 |
|         |        |      | 3-23-01 | 3-16-01 | 4-01 |
|         |        |      | 3-23-01 | 3-16-01 | 4-02 |
|         |        |      | 3-23-01 | 4-17-01 | 4-02 |
|         |        |      | 3-23-01 | 5-5-01 | 1-01 |
|         |        |      | 3-23-01 | 7-27-01 | 1-01 |
|         |        |      | 3-30-02 | 3-16-01 | 1-01 |
|         |        |      | 3-33-01 | 3-16-01 | 1-01 |
|         | 2 T    |      | 3-23-01 | 3-16-01 | 1-01 |
|         |        | NT   | 3-20-01 | 0-IR-01 | 1-01 |
|         |        |      | 3-23-01 | 1-14-01 | 1-01 |
|         |        |      | 3-23-01 | 2-2-01 | 1-01 |
|         |        |      | 3-23-01 | 2-OF15-2 | 1-01 (1) |
|         |        |      | 3-23-01 | 2-OF15-2 | 1-01 (2) |
|         |        |      | 3-23-01 | 3-3-01 | 1-01 |
|         |        |      | 3-23-01 | 3-9-01 | 4-02 |
|         |        |      | 3-23-01 | 1-1-01 | 1-01 |
|         |        |      | 3-23-01 | 1-7-01 | 1-01 |
|         |        |      | 3-23-01 | 1-14-01 | 1-01 |
|         |        |      | 3-23-01 | 1-26-01 | 4-02 |
|         |        |      | 3-23-01 | 1-IR1-01 | 1-01 (1) |
|         |        |      | 3-23-01 | 1-IR1-01 | 1-01 (2) |
|         |        |      | 3-23-01 | 1-IR1-01 | 1-01 (3) |
|         |        |      | 3-23-01 | 1-IR1-01 | 4-02 (1) |
|         |        |      | 3-23-01 | 1-IR1-01 | 4-02 (2) |
|         |        |      | 3-23-01 | 2-2-01 | 1-01 |
|         |        |      | 3-23-01 | 2-2-01 | 4-02 |
|         |        |      | 3-23-01 | 2-IR2-01 | 4-02 |
|         |        |      | 3-23-01 | 2-OF15-2 | 1-01 (1) |
|         |        |      | 3-23-01 | 2-OF15-2 | 1-01 (2) |
|         |        |      | 3-23-01 | 3-9-01 | 4-02 (1) |
|         |        |      | 3-23-01 | 3-9-01 | 4-02 (2) |
|         |        |      | 3-23-01 | 3-10-01 | 1-01 |
|         |        |      | 3-23-01 | 3-16-01 | 3-02 (1) |
|         |        |      | 3-23-01 | 3-16-01 | 3-02 (2) |
|         |        |      | 3-23-01 | 3-16-01 | 4-01 |
|         |        |      | 3-23-01 | 3-16-01 | 4-02 |
|         |        |      | 3-23-01 | 3-22-01 | 1-01 |
|         | 1 T    |      | 3-23-01 | 3-16-01 | 1-01 |
|         |        | NT   | 3-20-01 | 3-16-01 | 1-01 |
|         |        |      | 3-23-01 | 0-IR-01 | 1-01 |
|         |        |      | 3-23-01 | 0-IR-01 | 4-02 |
|         |        |      | 3-23-01 | 0-IR-01C | 1-01 |
|         |        |      | 3-23-01 | 0-IR-01C | 5-02 |
|         |        |      | 3-23-01 | 1-1-01 | 1-01 |
|         |        |      | 3-23-01 | 1-7-01 | 1-01 |
|         |        |      | 3-23-01 | 1-14-01 | 1-01 |
|         |        |      | 3-23-01 | 1-26-01 | 4-02 |
|         |        |      | 3-23-01 | 1-IR1-01 | 1-01 (1) |
|         |        |      | 3-23-01 | 1-IR1-01 | 1-01 (2) |
|         |        |      | 3-23-01 | 1-IR1-01 | 1-01 (3) |
|         |        |      | 3-23-01 | 1-IR1-01 | 4-02 (1) |
|         |        |      | 3-23-01 | 1-IR1-01 | 4-02 (2) |
|         |        |      | 3-23-01 | 2-2-01 | 1-01 |
|         |        |      | 3-23-01 | 2-2-01 | 4-02 |
|         |        |      | 3-23-01 | 2-IR2-01 | 4-02 |
|         |        |      | 3-23-01 | 2-OF15-2 | 1-01 (1) |
|         |        |      | 3-23-01 | 2-OF15-2 | 1-01 (2) |
|         |        |      | 3-23-01 | 3-9-01 | 4-02 (1) |
|         |        |      | 3-23-01 | 3-9-01 | 4-02 (2) |
|         |        |      | 3-23-01 | 3-10-01 | 1-01 |
|         |        |      | 3-23-01 | 3-16-01 | 3-02 (1) |
|         |        |      | 3-23-01 | 3-16-01 | 3-02 (2) |
|         |        |      | 3-23-01 | 3-16-01 | 4-01 |
|         |        |      | 3-23-01 | 3-16-01 | 4-02 |
|         |        |      | 3-23-01 | 3-22-01 | 1-01 |
| Comparison                        | p-value (χ² test) |
|----------------------------------|------------------|
| Pt1 tumor Vs non-tumor           | 9*E-08           |
| Pt2 tumor Vs non-tumor           | 4.3*E-4          |
| Pt3 tumor Vs non-tumor           | 4*E-15           |
| Pt1 tumor Vs Pt2 tumor           | 0.004            |
| Pt1 tumor Vs Pt3 tumor           | 0.02             |
| Pt2 tumor Vs Pt3 tumor           | 0.39             |

*This Table lists the SoDA output, before manual examination. When there were two or more clones with the same V(D)J segments (but different in CDR3), they are marked with numbers – (1), (2), etc.

Table S5: Significance of differences in mutation distributions across different patients (χ² test)
**Table S6:** Significance of differences in mutation distributions across the different samples from the same patient ($\chi^2$ test)

| Patient No. | Comparison                        | p-value ($\chi^2$ test) |
|-------------|-----------------------------------|-------------------------|
| 1           | Sample 3 tumor Vs Sample 2 tumor   | 0.88                    |
|             | Sample 3 tumor Vs Sample 1 tumor   | 0.845                   |
|             | Sample 3 tumor Vs non-tumor        | 0.014                   |
|             | Sample 2 tumor Vs non-tumor        | 1.5*E-05                |
|             | Sample 1 tumor Vs non-tumor        | 1.5*E-04                |
| 2           | Sample 1 tumor Vs Sample 2 tumor   | 0.024                   |
|             | Sample 2 tumor Vs non-tumor        | 0.022                   |
|             | Sample 1 tumor Vs non-tumor        | 0.10                    |
| 3           | Sample 1 tumor Vs Sample 2 tumor   | 0.046                   |
|             | Sample 2 tumor Vs non-tumor        | 7.7E-17                 |
|             | Sample 1 tumor Vs non-tumor        | 0.04                    |

**Table S7:** Numbers of transition and transversion mutations in tumor and non-tumor clones across all FL patients, and in normal GCs

| Sample   | Number of mutations | p-value- ($\chi^2$ test) |
|----------|---------------------|-------------------------|
|          | Transitions         | Transversions           |
| Pt1      | T                   | 417                     | 504                     | 0.58          |
|          | NT                  | 491                     | 531                     |               |
| Pt2      | T                   | 526                     | 489                     | 0.08          |
|          | NT                  | 214                     | 141                     |               |
| Pt3      | T                   | 567                     | 790                     | 0.60          |
|          | NT                  | 230                     | 356                     |               |
| FL-S     |                     | 1496                    | 1117                    |               |
| Normal GCs |                   | 367                     | 289                     |               |

**Table S8:** Numbers of transition and transversion mutations in tumor and non-tumor clones across each sample from FL-HTS patients

| Patient and sample | Number of mutations | p-value- ($\chi^2$ test) |
|--------------------|---------------------|-------------------------|
|                    | Transitions         | Transversions           |
| Pt1                | Sample 3            | T                      | 109                     | 154           | 0.051        |
|                    |                     | NT                     | 279                     | 266           |              |
|                    | Sample 2            | T                      | 80                      | 147           | 0.0014       |
|                    |                     | NT                     | 191                     | 182           |              |
|                    | Sample 1            | T                      | 164                     | 204           | 0.25         |
|                    |                     | NT                     | 367                     | 362           |              |
| Pt2                | Sample 2            | T                      | 120                     | 125           | 0.001        |
|                    |                     | NT                     | 163                     | 89            |              |
|                    | Sample 1            | T                      | 350                     | 267           | 0.22         |
|                    |                     | NT                     | 114                     | 68            |              |
| Pt3                | Sample 2            | T                      | 144                     | 294           | 0.17         |
|                    |                     | NT                     | 175                     | 267           |              |
|                    | Sample 1            | T                      | 385                     | 427           | 0.08         |
|                    |                     | NT                     | 68                      | 107           |              |
**Table S9:** Numbers of positions in AID targeting motifs with significant differences between tumor and non-tumor clones in each sample

| Patient 1 | Patient 2 | Patient 3 |
|-----------|-----------|-----------|
| Sample 3 T-NT | Sample 2 T-NT | Sample 1 T-NT |
| 44 | 49 | 55 |
| Sample 2 T-NT | Sample 1 T-NT | Sample 2 T-NT |
| 87 | 103 | 87 |
| Sample 1 T-NT | Sample 2 T-NT | Sample 1 T-NT |
| 98 | 98 | 98 |

**Table S10:** Numbers of positions in AID targeting motifs with significant differences between different tumors in each patient

| Patient 1 | Patient 2 | Patient 3 |
|-----------|-----------|-----------|
| Sample 3 T-sample 2 T | Sample 3 T-sample 1 T | Sample 2 T-sample 1 T |
| 21 | 23 | 40 |
| Sample 2 T-sample 1 T | Sample 2 T-sample 1 T |
| 47 | 47 |

**Table S11:** Numbers of mutations in AID targeting motifs around each nucleotide, in tumor and non-tumor clones from FL patients and normal GCs

| Sample | Number of mutations in motif |
|--------|-----------------------------|
|        | A  | C  | G  | T  |
| Pt1 T  | 126 | 106 | 64 | 54 |
| NT     | 161 | 111 | 143 | 46 |
| Pt2 T  | 100 | 60  | 101 | 117 |
| NT     | 35  | 48  | 64  | 38 |
| Pt3 T  | 136 | 102 | 142 | 91 |
| NT     | 84  | 28  | 69  | 51 |
| FL-S   | 351 | 272 | 303 | 193 |
| Normal GCs | 77 | 69  | 81  | 65 |

**Table S12:** Numbers of mutations in AID targeting motifs around each nucleotide, in tumor and non-tumor clones in each sample from the FL-HTS patients

| Patient and sample | Number of mutations in motif |
|--------------------|-----------------------------|
|                    | A  | C  | G  | T  |
| Pt1 Sample 3 T     | 31 | 23 | 24 | 12 |
| NT                 | 88 | 66 | 94 | 18 |
| Sample 2 T         | 23 | 21 | 15 | 8  |
| NT                 | 57 | 50 | 82 | 4  |
| Sample 1 T         | 42 | 41 | 27 | 15 |
| NT                 | 111 | 84 | 118 | 19 |
| Pt2 Sample 2 T     | 33 | 19 | 20 | 23 |
| NT                 | 26 | 41 | 45 | 21 |
| Sample 1 T         | 41 | 32 | 40 | 74 |
| NT                 | 19 | 22 | 30 | 24 |
| Pt3 Sample 2 T     | 39 | 42 | 33 | 25 |
| NT                 | 73 | 20 | 52 | 41 |
| Sample 1 T         | 67 | 61 | 79 | 53 |
| NT                 | 17 | 9  | 21 | 13 |
**Table S13**: Significance of the differences in percentages of the number of PGS and potential AGS in GL ($\chi^2$ test)*

| Patient / Sample                  | Vs. patient / sample | p-value ($\chi^2$ test) |
|-----------------------------------|----------------------|-------------------------|
| 1 (samples 3+2)                   | 2                    | 0.0013                  |
| 1 (samples 2+1)                   | 2                    | 0.0013                  |
| 1 (samples 3+1)                   | 2                    | 0.0017                  |
| 1 (samples 3+2)                   | 1                    | 0.28                    |
| 1 (samples 2+1)                   | 1                    | 0.23                    |
| 1 (samples 3+1)                   | 1                    | 0.27                    |
| 2                                 | 3                    | 0.0008                  |
| 1 Tumor (samples 3+2)             | 2 Tumor              | 0.0017                  |
| 1 Tumor (samples 2+1)             | 2 Tumor              | 0.0017                  |
| 1 Tumor (samples 3+1)             | 2 Tumor              | 0.0017                  |
| 1 Tumor (samples 3+2)             | 3 Tumor              | 0.375                   |
| 1 Tumor (samples 2+1)             | 3 Tumor              | 0.375                   |
| 1 Tumor (samples 3+1)             | 3 Tumor              | 0.375                   |
| 2 Tumor                           | 3 Tumor              | 0.008                   |

*As Patients 2 and 3 had two samples each and patient 1 had three samples, we performed the $\chi^2$ test for patients 2 and 3 twice, each time with each couple of samples from patient 1.