Appendix 1

A

IGHV1-69 SLE1
```
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYTISWVRQAPGQGLEWMGRIIPILGIANYAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCAR
...................                   .........................    ...............................
R...........                    A.....            ......TP.....    ...SV.T.R    ....VTAA..........
 .......S...                ....A.....            .....M.....      ...SV.T.K
..H.........           ...Y..TT.D.H...
```

IGHV1-69 SLE2
```
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYTISWVRQAPGQGLEWMGRIIPILGIANYAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCAR
............                          .........................    ...............................
                                      ........Q...    ..T......    .................R
                                      .........V..                 ................R
                                      .......Q....                 .........R
                       .......N.......     ....V..                 ........R ....D.....
                       .......NN......     ....L..                            .S.......
                       ....S..N..VG...                     ...N....           ....V....
                                                                   ...SV.T.R
                                                                   ..M.E.T.H...........
                                                                   ..M.E.T.............
```

IGHV1-69 SLE3
```
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYTISWVRQAPGQGLEWMGRIIPILGIANYAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCAR
............           ........................................    ....................
..L.........           .D.............            ....F.T......    .........R     ...VTAA.....
   ........T.......    ..D............         KSM..DVY.....RR     ......A..R
                       ........FV.A...            ......ML.....    ......E..N..........
                       ..N.P..........            ....FET......    ......E..R
                       .........A.....     ....V..                            .T........
                                           ....L..
```

IGHV1-69 SLE4
```
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYTISWVRQAPGQGLEWMGRIIPILGIANYAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCAR
............                          ..........                              .....R
                                           ....V..
                                           ....L..
```

IGHV1-69 SLE5
```
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYTISWVRQAPGQGLEWMGRIIPILGIANYAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCAR
...................                          ..........            ....................
...........R                                                       .V..................
   NP.T....QL.AR                                                   ..S.................
                                                                   .........T..........
                                                                   ......EP.T..........
                                                                   ......E.............
                                                                         .P............
                                                                   ...SV.T.K           .D.......P.
```

IGHV1-69 SLE6
```
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYTISWVRQAPGQGLEWMGRIIPILGIANYAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCAR
............               .......................                       ..............
            .......                        ....L..
```

B

IGHV3-7 SLE1
```
EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
...........................                .........      .......           ......................
..H..........      ...........             .V..SR                           .T.........
.........D.........                                                                    ....L.....K
.........D..K......                                                                   L....L.....K
                                                                                      V....L.....K
```

IGHV3-7 SLE2
```
EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
..........................P..R .......     ......................           ......................
..H................        ...N.E.N...     ......F.R                        .......D...
.G.................                                                         .T......  ..D.........
...V...............                                                         .T.F.... .TS..........
...P...............                                                                    TD.........
.........D.........                                                                    ...M.......
..........S........
...........E.......
....L....D.........
....L......G.......
 ...L......M....R
  ........V........
```

IGHV3-7 SLE3
```
EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
...................        ..DD.A.H...     .........                        ...........
.........D.........                        .....GF.R                        .T.........
.........H.........                                                         .......D...
...P...........R                                                            .......DN..
```

IGHV3-7 SLE4
```
EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
...................             ......     .........
............K......                             .....HCPR
```

IGHV3-7 SLE5
```
EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
.............................              .........                        ...........
..........V........                        .....GF.R                        .......D...
 .........V....R                                                                       SD.......P.
```

IGHV3-7 SLE6
```
EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
...................                        .........      ..A....           .T.....D...
                                           .V..SR                                    ............
```

C

IGKV2-28 SLE1
```
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP
............................................................................................
....................R   .......R            .............S.       .L...........
.............S..........                                          ..A..........
        .....S..........                                          ..V..........
        .....A..........                                          ...V.........
                                                                  ....A........
                                                                  ....E........
                                                                  .....G.......
                                                                  .......L.....
                                                                  ........H....
                                                                  ........V....
                                                                  ........Y....
                                                                  ............E...
                                                                  .............N..
                                                                  Y............
                                                                  .....L.......
```

IGKV2-28 SLE2
```
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP
...........................................................       ..........................
.........Y......        .......R                                  ..A.....E....             ........
........D..A.SL..R                                                .............
                                                                  ......D......
                                                                  ........H....
                                                                  ............E...
                                                                  .............E.
```

IGKV2-28 SLE3
```
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP
............................................................................................
........D..A.SL..R                                                ............S...
        .....L.Q........
```

IGKV2-28 SLE4
```
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP
         ...............                                          .............
         ......WCSMR                                              ............T
```

IGKV2-28 SLE5
```
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP
......T.................                 ......A.......           .............   .......I..
........D..A.SL..R                                                .....A.......
         .S.............                                          .....A......R
         .S...L.Q.......
```

IGKV2-28 SLE6
```
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP
........................                          ....DV.T.       .............
........D..A.SL..R                                ....DA...
                                                  ....SN.Q.P......
```

D

IGKV3-20 SLE1
```
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP
..................      ................................................................
.....K............               .P...........         .A.....                ..............S.R
.V................              ..........K   .......TG.......                ..............RSN
............V.....      ...TI..-..N.......K   .....T...       ........H.......
.....H...N........      .......-N.......      .......T.       ........N.......
...M....A...V.....                            ....S....       ........A.......
                                              .....S...       C...............
                                           ..N....K           ..............T.
                                              ....W..T.       ..............R
                                              V...W....       .......A........
                                                              ....N..NTA......
                                                       .....V.
                                                              ........G.......
```

IGKV3-20 SLE2
```
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP
..................      ........................................................................
.V................      ...GI..-W.........K   V........       ..............N.
.F................      ...I.N.-..N.......K   ...D.....       ........H.......
........D.........      .......-N............         ..L.....
..............S...      ....I..-TW........K   ......L..
.....A............                            .....T...
.....K............              D.G.......K   ....W..T.
................D.                  ...L..T..K         T......
........A.........                                     P......
                                                       .....V.
```

IGKV3-20 SLE3
```
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP
..................               .......      ..........................................
.....K............      ....I..-W.........K   ............V...
 RQM....SS..A.V.D.      ....I.T-..........K   ..............C.
........A.........                            .............H.. FMV..........DK
.VL...............                            ....W..T.       ..............R
                                              ...F...T.       ..............-.
                                                              ....E.........R
                                                              ..........S.....
                                                              ............S...
```

IGKV3-20 SLE4
```
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP
..................               .............         .................................
      ....V.......
   LS....NR
    LS...DNR
```

IGKV3-20 SLE5
```
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP
..................             L.N......      .........       ..........................
```

```
.....K............                                A...LQS.V.S.
.......SA.M.......
```

IGKV3-20 SLE6

```
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP
..................                            ................................
.....K............                            .....T..........
                                              .....G.........
                                              ............H..
                                              ....W....
                                                  A...LQS.V.S.
                                              .............T.
```

E

Heavy joining peptides

```
IGHJ4 ..YFDYWGQGTLVTVSS                    IGHJ6 ...YGMDVWGQGTTVTVSS
SLE1        ...........                    SLE1     .-..............
               .A......                             ................
                                                 YYY.......K
SLE2    ...............                    SLE2       ..............
       G...............                            Y................
        L..............
          Y............

SLE3      AH...........                    SLE3      ...............
           ............
           .....S......
          PET..........
SLE4       ............                    SLE4     .-.....K

SLE5    ...L..R                            SLE5        TL...........
               ........                              ...............
              R........                              E..............
        D..............                            Y.-..............
        ...L..R                                   GRG...............
       GT..N..R........

SLE6      .............                    SLE6             ........
```

Kappa joining peptides

```
IGKJ2....YTFGQGTKLEIK                      IGKJ4......LTFGGGTKVEIK

SLE1     L......R                          SLE1    SYP........
         .......                                DSSSDPVV......
       LPI......R

SLE2  GSSP.......                          SLE2   SNWP........
      QTPP.......                                 STWP........
      SFPW.......                                  GWV........

SLE3    CS...........                      SLE3      P.........
         L.......V.                                QTP.........

SLE4     ..........                        SLE4       .........

SLE5   FP........                          SLE5    THP..........

SLE6       ......                          SLE6          ......
```

Supplementary figure 1. *De novo* sequencing of affinity-purified anti-SmD IgGs from 6 patients with systemic lupus erythematosus (SLE) reveals clonal restriction with common heavy (H)- and light (L)- chain variable (V)- and joining (J)- regions. **A.** IGHV1-69 gene family usage. **B.** IGHV3-7 gene family usage. **C.** IGKV2-28 gene family usage. **D.** IGKV3-20 gene family usage. A number of public V-region mutations were identified which are tabulated by proteomic heat map in Figure 3. A number of privately mutated peptides within each affinity-purified anti-SmD IgG sample were also sequenced. **E**. Sequencing of J-regions reveals an IGHJ4, IGHJ6, IGKJ2, and IGKJ4. Dots indicate homology with the germline sequence derived from the ImMunoGeneTics database; mutations divergent from germline are indicated in text; germline complementary determining regions are underlined; - indicates deletion; spaces indicate areas of incomplete sequence.