

## Appendix 2

### A

IGHV3-7 SLE1

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR

..... A.H... ..  
.....C.....K..... AL.... ..GR ..R .DSE.TA.....K  
.....D..... ..N..... .TA.....K  
.....N....E...K ..Q....N..... ..E.....  
.....F.K..... ..N....TH..... ..N.....  
.....V..... ..E... .TSD.....T.  
.....N..... .TSD.....NM.  
.....M.... ..K  
.....ST..A.... ..L...T.  
.....T..A....  
.....A....

IGHV3-7 SLE2

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR

.....  
.....H..... T..... ..GR STF.A.... ..Y. .T.....  
.....L..... ..N.....  
.....R ...T.....K TF.E.... ..GAFD.DK  
.....T.....R S.A.... ..K ..  
MFGV.....K ..A.... ..K  
.....F..... W....ASCYR  
.....F..... ..N.....S  
.....N.....R VD.....APK  
.....N..... EA...N....  
.....I..A.... VSF.....  
.....L..... V.....T.  
.....L...T.

IGHV3-7 SLE3

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR

.....  
..AF.....V....R ...T.....R ..GR QDGV... ..  
.....T.....SGNHSR

IGHV3-7 SLE4

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR

..... A.H... ..  
NTAYL.L..... ..GR .GTT..A.... ..

```

..... TF.A.... TT.....
..... T..A.... .T...K.D...
.....K N..... SQ.....P..K
.....NR
.....R V.....AH.DR
.....K V.....K
V.....STDK

```

A.....TM.K

```

ETD...F.EK
TED.....TVLTR

```

IGHV3-7 SLE5

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWM~~SWVRQAPGKLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR~~

```

..... A.H... ..
..H.....K Y.H... ..GR ..E...T..
.....K S.N... ..T.... Q.....REK
.....D.....K..... ..SS.SSR ..R ..V.....
.....SS.TTR .YI..A.... .T.....
.....SS.SGR .....E.. .....S..
AV...SS.SGR F..... .....T.
.....SS...K ST..... .....TM..
.GST..... V.....TM..
.....F.T.

```

IGHV3-7 SLE6

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWM~~SWVRQAPGKLEWVANIKQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR~~

```

..... NA..... ..Ä.... .T.....
..L..... A..... ..GL.. TS.A.... .T..... .....S
.....D..... .S.T... ..ST.SGR .Q..... .T.F...DR S.....S
.....F..... ..SG.SGR NA..... .....MGGYDK
.TG...GLGS..... ..SA.SGR
.....R ..SGP.....TK GASHSTS.A....
.....R FEN.T.....K S.VNTD.A....

```

**B**

IGH1-3 SLE1

QVQLVQSGAEVKKPGASVKVSKASGYTF~~TSYAMHWVRQAPGQRLEWGMGINAGNGNTKYSQRFQGRVTITTRDTSASTAYMELSSLRSEDTAVYYCAR~~

```

.....
..P..... ..R .....T.....V.....
..P..... ..LSR .LS... ..L...T.....G...

```

EAF.....R .L....K .....V.

SYP.....R .....T. ....G....I..PSG. ..LE.... ES.L....D.R .....

.....CMDK .....G....R ...L.... .A.....

.....WGDK .....G....L.R ...Q..D. .D.....T.

...Q.... .T.D.....T.

...N..N. .T.D.....NM.

...N.E..

...N..A.

...N..D.

...N..K

...N....

...NL...

...D....

...S....

...T....

...W..M..

...DW..N..

IGH1-3 SLE2

QVQLVQSGAEVKKPGASVKVSKASGYTFSTYAMHWVRQAPGQRLEWGMWINAGNGNTKYSQKFGQGRVTITRDTSASTAYMELSSLRSEDTAVYYCAR

.....K .....N..D. V..T.....

NL.....G....R ...N..A.

.....R .....T. ...NL...

.....T... ..GSDG.R ...N.... ...N.....

.....

...T....

...T..D.

...T..DK

...TL..DK

...D....

...S....

...E....

...FQ...

IGH1-3 SLE3

QVQLVQSGAEVKKPGASVKVSKASGYTFSTYAMHWVRQAPGQRLEWGMWINAGNGNTKYSQKFGQGRVTITRDTSASTAYMELSSLRSEDTAVYYCAR

.....G....R ...N....

SPPGLAH.....EK .....N..D. ...N.....

.....K ...T.... .....D.....

.S\_.....R ...Q..D. ....G..

.....T. ...Q.... .....

.....CSMR ...D.... .L.....K

...FQ... T.....SGNHSR

IGH1-3 SLE4

QVQLVQSGAEVKKPGASVKVSKASGYTFTSYAMHWVRQAPGQRLEWMGWINAGNGNTKYSQKFKQGRVTITRDTTSASTAYMELSSLRSEDTAVYYCAR

.....N.....

PL.....K.....N..D.....K

.....NR.....Q.....VTAA.....

.....R.....S.NA.....

.....R.....V.....STD.

.....CTMK.....V.....K

.....V.....AH.DR

.....F.....

.....A.....TMAK

.....ET.....F.EK

.....MV.....TVLTR

.....TVLTR

.....L.....

IGH1-3 SLE5

QVQLVQSGAEVKKPGASVKVSKASGYTFTSYAMHWVRQAPGQRLEWMGWINAGNGNTKYSQKFKQGRVTITRDTTSASTAYMELSSLRSEDTAVYYCAR

.....GH.....G.....R.....N.....

.....G.....D.YI.....PNS.G.N.A.....T.....

.NNDATAY.....I.....R.....

.....Y.....I.....L...R.....T.

.....I.....V.R A.....T.

.....R A.....TM..

.....V.....TM..

.....V.....SCAR

IGH1-3 SLE6

QVQLVQSGAEVKKPGASVKVSKASGYTFTSYAMHWVRQAPGQRLEWMGWINAGNGNTKYSQKFKQGRVTITRDTTSASTAYMELSSLRSEDTAVYYCAR

EAF.....L..R.....N.AN.....K

.....NYATEY.....EN.....T.....K

.....NL... N.L...L.K.....

.....W..M.. A.....MGGYDK

C

IGKV3-20 SLE1

EIVLTQSPGTLISLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPARFSGSGSDTFTLTISRLEPEDFAVYYCQQYGSSE

.....V.....N.....F.....G.....

.....A.....T.....D.....

.....A.....H.....S.....

```

.....A.....          ....D..T.          .....S.....QS
.....V.....          ....D..N.          .....N...N...
.....L.....          .....A...D.          .....DC.K
.....D.....          .....T.          .....N...
          .....LCK          .....N.
          .....CVK          .....V...
          .....DK          .....V..
          ..N...K          .....A.AVLMYR
          .....LHVR

```

IGKV3-20 SLE2

EIVLTQSPGTL<sup>S</sup>SLSPGERATL<sup>S</sup>CRASQ<sup>S</sup>VSSSYLAWYQ<sup>K</sup>QKPGQAPRLLIY<sup>G</sup>ASSRATGIPARFSGSGSGTDFTLTISRLEPEDFAVY<sup>C</sup>Q<sup>Q</sup>Y<sup>G</sup>S<sup>S</sup>P

```

.....          .....          .....          .....          .S.....R
.....D.....          .....SR          ..M.S....          V.....
.....D.V.....          QF.....DK          .....MG..          .....S.....
.....V.....          .....          .....D.          .....E.....LAR
.....A.....          ..N.....K          ..P...D.          .....
.....S.....          .....K          ...D..N.          .....L.....
.....S.....          LS.....          ...F...T.          .....S...
.....D.....          .....          .....T.T.          .....T.
..A..DSR          .....          .....T.          .....L.
          .....          .....W..T.          .....N.
          .....          ...A..T.          S.....K
          ..N...K

```

IGKV3-20 SLE3

EIVLTQSPGTL<sup>S</sup>SLSPGERATL<sup>S</sup>CRASQ<sup>S</sup>VSSSYLAWYQ<sup>K</sup>QKPGQAPRLLIY<sup>G</sup>ASSRATGIPARFSGSGSGTDFTLTISRLEPEDFAVY<sup>C</sup>Q<sup>Q</sup>Y<sup>G</sup>S<sup>S</sup>P

```

.....          .....          .....          .....          EPDQAP.....R
.....A.....          N.....PK          .....D.          EPDAPQ.....R
.....S.....          N.....          ....._          .....S.....
.....D.....          .....PK          ..D....          S.....K
S.....NDK          .....V.V...K          .....V...
S.....NSR          .....V.V..K          .....N...
S.....DSR          ..M....LQSRPSR LLLP.....
          .....T.          .....S...
          .....W..T.          .....N.
          .....          L.....K
          .....          .....K
          .....          .....R
          .....          .....R

```

IGKV3-20 SLE4

EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPARFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP

```

.....D.      S.....K      .....TPFANSK
.....F.....      .....      VLDE.....  _...A__CO_.....PTFGNTK
.....S.....      .....R      .A...D.  VCTYSLSS.....K      TNSNS.....YTFGATNK
.....A.....      .....      ..D..D.  TTTYSLSS.....K
.....A..V.....      .....      ...D..T.  .....
LV.....DDK      .....G.....R      ...DT...  .....S.....
S.....NSR      .....G.TN.SVR      ...W..T.  .....V....
V.....      .....T..  .....N...
.....V..
.....N.

```

IGKV3-20 SLE5

EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPARFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP

```

.....
.....A.....      .N.....      .....
.V.....      .....      ...D...
.....D.....      .....      ...D..N.
..A..DSR      .....T.
..D....

```

IGKV3-20 SLE6

EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPARFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP

```

.....N.....      .....A.....
.V.....      .....      ...D.
...F.....      N.AYLNVS.....K  F.....      .....K_.....
.....K.....      .....AGK  ..N...K      .....E.....
.....A.....      .....T.  HP.....A.....
.....P....      .....      HP.....S....K
DV.....R      V.....      KY.....E.DK
.....V.SVP.      .....      KY.....DK
.....      .....MATYSLSS.....K
.....      .....TTYSLSS.....K
.....AVEVPAPGQR

```

D

IGKV1-39 SLE1

DIQMTQSPSSLSASVGRVTITCRASQSISSYLWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQSYSTP

```

.....      .....N....K      .....R

```

.....A.....H.....N.....  
.....R.....SR.....N.....  
MG.....

.....  
.....G.....  
.....E.....  
.....G.....  
.....G.....  
.....G.....  
.....S..T...S..  
.....S.....  
.....S...S.....  
.....T.....  
.....T.....  
.....T.....  
.....T.....  
.....TT.N.....  
.....N.....  
.....F.....  
.....FG.....  
.....G.....  
V...G.....  
V.....  
V...SSSS.....  
.....V.....  
.....M.....  
.....W.....  
.....R

IGKV1-39 SLE2

DIQMTQSPSSLSASVGRVITCRASQSISSYLNWYQQKPGKAPKLLIYAASLQSGVPSRFRFGSGSGTDFTLTISSLPEDFATYYCQQSYSTP

..... .S...YG.S.R  
MG..... .N...K .....R  
.....Q...K .....S...R  
.....F..... S....K  
.....G.....  
.....S..T...S..  
.....S.K .....L.S..R  
.....S...R  
.....NR

....E.....  
...FE.....  
...TVE.....  
...TE.....  
...G.....  
VT.....  
VT.....DK  
TGALSG.....

IGKV1-39 SLE3

DIQMTQSPSSLSASVGRVITTCRASQSISSYLNWYQQKPKGKAPKLLIYAASSLQSGVPSRFRFGSGSGTDFTLTISSLPEDFATYYCQQSYSTP

.....  
MG.....R  
T.....R  
T....NM\_... V..... KY.....R  
STS..... V...\_Q..... LLLP.....R  
Q..... S.....K  
..V.....  
..V.G.....  
..V.E.....  
....V.....  
.....R  
.....SE.....R  
L.....K  
...T.....K  
..M.G.....  
..M.G.....P.  
..M..G.....  
...G....T....  
...GY.....SP.  
.....T....  
..T.....  
T.N.....  
.....R  
...F.....  
...S.....

IGKV1-39 SLE4

DIQMTQSPSSLSASVGRVITTCRASQSISSYLNWYQQKPKGKAPKLLIYAASSLQSGVPSRFRFGSGSGTDFTLTISSLPEDFATYYCQQSYSTP

..... S.....K  
.....R ..... .V.....



VE.....R L..... .V.....  
 .....K..... .K..... .V.....AL.  
 NYLARN.....PCK .....T.....  
 .....VY....DK  
 .....T.....  
 .....K.....  
 .....QTK  
 .....WK

IGKV1-39 SLE5

DIQMTQSPSSLSASVGRVITICRASQSISSYLNWYQQKPKGKAPKLLIYAASSLQSGVPSRFRFGSGSGTDFTLTISSLPEDFATYYCQQSYSTP

..... S....K  
 .....T.....  
 ....S..T....S..  
 MV.....K  
 .....A...K  
 ....A.....K  
 V...T.....  
 V...G.....  
 ...G.....  
 .V.....  
 ....E.E....  
 ....E.....  
 .....G....  
 .....L..  
 ...S.....  
 .....N.....  
 ..N.....  
 N.....

IGKV1-39 SLE6

DIQMTQSPSSLSASVGRVITICRASQSISSYLNWYQQKPKGKAPKLLIYAASSLQSGVPSRFRFGSGSGTDFTLTISSLPEDFATYYCQQSYSTP

..... NSAYLNSV..... KY.....DK  
 .....K Q..Q..QV.. ..T.....K KY.....E.DK  
 ..... AMTYSLSS.....K  
 TTYSLSS.....K  
 .....K.....R  
 HP....A.....R  
 HP.....K  
 ....AEVPAPGQR

**E**

Heavy joining peptides

IGHJ4 ..YFDYWGQGLVTVSS

SLE1 GV.....

.....

.....

.L.....

...S.....

SLE2 .....

.....

FWSP.....

SLE3 .....

.....

SLE4 .....

P.....

SLE5 .....

SA.....

T.....

.A.....

Q.....

AF.....

F.....

SLE6 WS.....

S.....

NA.....

P.....

.....

C.....

CL.....

AME.....

IGHJ6 ...YGM DVWGQGT TTVTVSS

SLE1 .....

.....

SLE2 .....

.....

SLE3 .....

SLE4 .....

SLE5 L.....

.....

NA.....

SLE6 .....

**F**

Kappa joining peptides

IGKJ2 ....YTFGQGTKLEIK

SLE1 SPL.....

SP.....

PP.....

.....R

LNKS...K

SSPQ....SK

SPQ.....

QTPI.....R

QAPI.....R

QSPI.....R

TPQ.....

LSPQ.....

NTPL.....R

NTPL..\_W..R

NVPL.....R

APL...SQK

SPL...WK

SLE2 .....NV.F.

.....TV...

.....QV...

.....E.

NTPQ.....R

TP.....

SSPQ.....S.

IGKJ2 ....YTFGQGTKLEIK (cont.)

SLE3 STPQ.....  
.....N....  
.....R  
...P...  
NSPP...N\_..  
TSP.....  
SSPQ.....  
SSPQ.....S.  
.....E.  
.....  
SPL...N\_..  
SLE4 SYP.....  
TPF...P...  
YNSAP.....  
GSSP.....R  
STPQ.....  
YGSSP...ATNK  
YGSSPP...NTK  
SLE5 ...P...  
.....R  
TPL...WK  
.....TV...  
G...P...  
FS...T...  
SSPI.....R  
TP.....  
SYPL.....  
TPI.....R  
QTPI.....R  
SLE6 F...P...  
FP.....R  
SPV.....  
SPV.....QV...  
WPA.....

IGKJ4 ....LTFGGGTKVEIK  
SLE1 NTP.....  
EW..Q...R  
QALQTP.....  
SVP.....  
SSPP.....  
SP.....  
P.....  
SLE2 YNTYP.....  
SLE3 NNHWV.....  
SP.....  
SLE4 SNP.....  
SLE5 SP.....  
TSP.....  
SLE6 .....

Supplementary figure 2. *De novo* sequencing of affinity-purified anti-Rib-P IgGs from six patients with systemic lupus erythematosus (SLE) reveals clonal restriction with common heavy (H)- and light (L)- chain variable (V)- and joining (J)- regions. **A.** IGHV3-7 gene family usage. **B.** IGHV1-3 gene family usage. **C.** IGKV3-20 gene family usage. **D.** IGKV1-39 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-Rib-P IgG sample were also sequenced. **E.** Sequencing of JH-regions reveals an IGHJ4 and IGHJ6. **F.** Sequencing of JK-regions reveals an 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.