SEQUENCE LISTING

<110> ACADEMIA SINICA

<120> ANTI-VEGFR2 HUMAN ANTIBODY FOR ANTI-ANGIOGENIC AND TARGETED CANCER THERAPY

<130> 10011-051PCT

<150> 62147344
<151> 2015-04-14

<160> 80

<170> PatentIn version 3.5

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Asp Asp Ile Ile Asn Tyr
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Gln Gln Tyr Asp Ile Leu Pro Leu Thr
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Glu Phe Thr Phe Ser His Tyr Asn
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Ile Ser Asp Asp Gly Arg Asn Lys
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Gln Ser Val Gly Ser Tyr
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His Gln Ser Ser Ser Leu Pro Arg Thr
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Gly Gly Asn Phe Ile Ser Lys Gly
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Ile Ile Pro Leu Phe Gly Thr Gly
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Gln Gln Ser Tyr Ser Thr Pro Leu
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Gly Phe Thr Phe Ser Ser Tyr Ala
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His Gln Ser Tyr Ser Ala Pro Pro Thr
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Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser
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Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser
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Ser

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Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
1 5 10 15

Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
20 25 30

Thr Ala Val Tyr Tyr Cys
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Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
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Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
20 25

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Leu Asn Trp Tyr Gln His Lys Ser Gly Glu Asp Pro Lys Leu Leu Ile
1 5 10 15

Tyr

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Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
1 5 10 15

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
20 25 30

Thr Tyr Tyr Cys
35

<210> 33
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Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
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Gln Val Asn Leu Arg Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser
20 25

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Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
1 5 10 15

Ser

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Phe Tyr Thr Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
1 5 10 15

Ser Arg Ser Ser Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
20 25 30

Thr Ala Ile Tyr Tyr Cys
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Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
1 5 10

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser
20 25

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Leu Asn Trp Tyr Gln Gln Lys Pro Gly Glu Ala Pro Lys Leu Leu Ile
1 5 10 15

Tyr

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Ile Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
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Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
20 25 30

Thr Tyr Tyr Cys
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<210> 41
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Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
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Glu Val Gln Leu Val Glu Ser Gly Gly Ala Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Val Gly Ser
20 25

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<400> 43

Leu His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu Ala
1 5 10 15

Val

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Tyr Tyr Gly Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
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Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp
20 25 30

Thr Ala Val Tyr Tyr Cys
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Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
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Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
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Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser
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Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu Leu Ile
1 5 10 15

Tyr

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Asn Arg Ala Thr Gly Val Ala Ala Arg Phe Ser Gly Ser Gly Ser Gly
1 5 10 15

Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Glu Ala Glu Asp Ala Ala
20 25 30

Thr Tyr Tyr Cys
35

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Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
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Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Met Lys Lys Ser Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
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Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
1 5 10 15

Gly

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Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Glu
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Ser Thr Thr Thr Val Tyr Leu Gln Leu Thr Ser Leu Thr Pro Glu Asp
20 25 30

Thr Ala Met Tyr Phe Cys
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Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
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Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
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Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
1 5 10 15

Tyr

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<400> 56

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Arg Gly Ser Gly Ser Gly
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Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
20 25 30

Thr Tyr Tyr Cys
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Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
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Gln Val Asn Leu Arg Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser
20 25

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<400> 59

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
1 5 10 15

Val

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Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
1 5 10 15

Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
20 25 30

Thr Ala Val Tyr Tyr Cys
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Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
20 25

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Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
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Tyr

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Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
1 5 10 15

Thr Asp Phe Thr Leu Thr Ile Asn Gly Leu Gln Pro Asp Asp Phe Ala
20 25 30

Ile Tyr Phe Cys
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Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
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Asn Trp Glu Tyr Pro Ser
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Thr Gln Ser Gly Ser Glu Met
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<210> 68
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Thr Trp His Ser Pro Pro
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<400> 69

Pro Phe Pro Gly Thr Val Ala
1 5

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gaacatttgg gaaatctctt gc 22

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Gln Gln Leu Asp Asp Ile Pro Ile Thr
1 5

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Met Gln Ser Lys Val Leu Leu Ala Val Ala Leu Trp Leu Cys Val Glu
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Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser Leu Asp Leu Pro
20 25 30

Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr
35 40 45

Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro

50 55 60

Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser
65 70 75 80

Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys Val Ile Gly Asn
85 90 95

Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser
100 105 110

Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser
115 120 125

Val Ser Asp Gln His Gly Val Val Tyr Ile Thr Glu Asn Lys Asn Lys
130 135 140

Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser
145 150 155 160

Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly Asn Arg
165 170 175

Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile
180 185 190

Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser
195 200 205

Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly Tyr Arg Ile Tyr
210 215 220

Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
225 230 235 240

Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile

245 250 255

Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
260 265 270

Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
275 280 285

Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu
290 295 300

Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
305 310 315 320

Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met
325 330 335

Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val Arg Ile Pro Ala
340 345 350

Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly
355 360 365

Ile Pro Leu Glu Ser Asn His Thr Ile Lys Ala Gly His Val Leu Thr
370 375 380

Ile Met Glu Val Ser Glu Arg Asp Thr Gly Asn Tyr Thr Val Ile Leu
385 390 395 400

Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val
405 410 415

Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val
420 425 430

Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr

435 440 445

Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu
450 455 460

Glu Cys Ala Asn Glu Pro Ser Gln Ala Val Ser Val Thr Asn Pro Tyr
465 470 475 480

Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys
485 490 495

Ile Glu Val Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys
500 505 510

Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr
515 520 525

Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser
530 535 540

Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln
545 550 555 560

Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser
565 570 575

Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro
580 585 590

Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr
595 600 605

Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile
610 615 620

Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr

625 630 635 640

Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val
645 650 655

Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn
660 665 670

Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys
675 680 685

Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn
690 695 700

Glu Thr Leu Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg
705 710 715 720

Asn Leu Thr Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Thr
725 730 735

Cys Gln Ala Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe
740 745 750

Ile Ile Glu Gly Ala Gln Glu Lys Thr Asn Leu Glu Ile Ile Ile Leu
755 760 765

Val Gly Thr Ala Val Ile Ala Met Phe Phe Trp Leu Leu Leu Val Ile
770 775 780

Ile Leu Arg Thr Val Lys Arg Ala Asn Gly Gly Glu Leu Lys Thr Gly
785 790 795 800

Tyr Leu Ser Ile Val Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His
805 810 815

Cys Glu Arg Leu Pro Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp

820 825 830

Arg Leu Lys Leu Gly Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val
835 840 845

Ile Glu Ala Asp Ala Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr
850 855 860

Val Ala Val Lys Met Leu Lys Glu Gly Ala Thr His Ser Glu His Arg
865 870 875 880

Ala Leu Met Ser Glu Leu Lys Ile Leu Ile His Ile Gly His His Leu
885 890 895

Asn Val Val Asn Leu Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu
900 905 910

Met Val Ile Val Glu Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu
915 920 925

Arg Ser Lys Arg Asn Glu Phe Val Pro Tyr Lys Thr Lys Gly Ala Arg
930 935 940

Phe Arg Gln Gly Lys Asp Tyr Val Gly Ala Ile Pro Val Asp Leu Lys
945 950 955 960

Arg Arg Leu Asp Ser Ile Thr Ser Ser Gln Ser Ser Ala Ser Ser Gly
965 970 975

Phe Val Glu Glu Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Ala Pro
980 985 990

Glu Asp Leu Tyr Lys Asp Phe Leu Thr Leu Glu His Leu Ile Cys Tyr
995 1000 1005

Ser Phe Gln Val Ala Lys Gly Met Glu Phe Leu Ala Ser Arg Lys

1010 1015 1020

Cys Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu
1025 1030 1035

Lys Asn Val Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile
1040 1045 1050

Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly Asp Ala Arg Leu Pro
1055 1060 1065

Leu Lys Trp Met Ala Pro Glu Thr Ile Phe Asp Arg Val Tyr Thr
1070 1075 1080

Ile Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile
1085 1090 1095

Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Lys Ile Asp Glu
1100 1105 1110

Glu Phe Cys Arg Arg Leu Lys Glu Gly Thr Arg Met Arg Ala Pro
1115 1120 1125

Asp Tyr Thr Thr Pro Glu Met Tyr Gln Thr Met Leu Asp Cys Trp
1130 1135 1140

His Gly Glu Pro Ser Gln Arg Pro Thr Phe Ser Glu Leu Val Glu
1145 1150 1155

His Leu Gly Asn Leu Leu Gln Ala Asn Ala Gln Gln Asp Gly Lys
1160 1165 1170

Asp Tyr Ile Val Leu Pro Ile Ser Glu Thr Leu Ser Met Glu Glu
1175 1180 1185

Asp Ser Gly Leu Ser Leu Pro Thr Ser Pro Val Ser Cys Met Glu

1190 1195 1200

Glu Glu Glu Val Cys Asp Pro Lys Phe His Tyr Asp Asn Thr Ala
1205 1210 1215

Gly Ile Ser Gln Tyr Leu Gln Asn Ser Lys Arg Lys Ser Arg Pro
1220 1225 1230

Val Ser Val Lys Thr Phe Glu Asp Ile Pro Leu Glu Glu Pro Glu
1235 1240 1245

Val Lys Val Ile Pro Asp Asp Asn Gln Thr Asp Ser Gly Met Val
1250 1255 1260

Leu Ala Ser Glu Glu Leu Lys Thr Leu Glu Asp Arg Thr Lys Leu
1265 1270 1275

Ser Pro Ser Phe Gly Gly Met Val Pro Ser Lys Ser Arg Glu Ser
1280 1285 1290

Val Ala Ser Glu Gly Ser Asn Gln Thr Ser Gly Tyr Gln Ser Gly
1295 1300 1305

Tyr His Ser Asp Asp Thr Asp Thr Thr Val Tyr Ser Ser Glu Glu
1310 1315 1320

Ala Glu Leu Leu Lys Leu Ile Glu Ile Gly Val Gln Thr Gly Ser
1325 1330 1335

Thr Ala Gln Ile Leu Gln Pro Asp Ser Gly Thr Thr Leu Ser Ser
1340 1345 1350

Pro Pro Val
1355

<210> 75

<211> 5
<212> PRT
<213> Homo sapiens

<400> 75

Gly Leu Met Thr Lys
1 5

<210> 76
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> VH region of R2S12 or R2S12-AF

<400> 76

Gln Val Asn Leu Arg Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Ser Tyr
20 25 30

Thr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser Ile Thr Ser Gly Ser Ser Tyr Ile Phe Tyr Thr Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Ser Ser Leu Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Ala Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
100 105 110

Val Thr Val Ser Ser
115

<210> 77
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> VL region of R2S12

<400> 77

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Asp Asp Ile Ile Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Glu Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Ile Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Ile Leu Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 78
<211> 107
<212> PRT
<213> Artificial Sequence

<220>

<223> VL region of R2S12AF

<400> 78

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Asp Asp Ile Ile Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Glu Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Ile Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Leu Asp Asp Ile Pro Ile
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 79
<211> 330
<212> PRT
<213> Homo sapiens

<400> 79

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser

35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu

225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 80
<211> 1340
<212> PRT
<213> Mus musculus

<400> 80

Met Glu Ser Lys Ala Leu Leu Ala Val Ala Leu Trp Phe Cys Val Glu
1 5 10 15

Thr Arg Ala Ala Ser Val Gly Leu Pro Gly Asp Phe Leu His Pro Pro
20 25 30

Lys Leu Ser Thr Gln Lys Asp Ile Leu Thr Ile Leu Ala Asn Thr Thr
35 40 45

Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro
50 55 60

Asn Ala Gln Arg Asp Ser Glu Glu Arg Val Leu Val Thr Glu Cys Gly
65 70 75 80

Gly Gly Asp Ser Ile Phe Cys Lys Thr Leu Thr Ile Pro Arg Val Val
85 90 95

Gly Asn Asp Thr Gly Ala Tyr Lys Cys Ser Tyr Arg Asp Val Asp Ile
100 105 110

Ala Ser Thr Val Tyr Val Tyr Val Arg Asp Tyr Arg Ser Pro Phe Ile
115 120 125

Ala Ser Val Ser Asp Gln His Gly Ile Val Tyr Ile Thr Glu Asn Lys
130 135 140

Asn Lys Thr Val Val Ile Pro Cys Arg Gly Ser Ile Ser Asn Leu Asn
145 150 155 160

Val Ser Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly
165 170 175

Asn Arg Ile Ser Trp Asp Ser Glu Ile Gly Phe Thr Leu Pro Ser Tyr
180 185 190

Met Ile Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp
195 200 205

Glu Thr Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly Val Ile
210 215 220

Leu Ser Pro Pro His Glu Ile Glu Leu Ser Ala Gly Glu Lys Leu Val
225 230 235 240

Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Leu Asp Phe Thr
245 250 255

Trp His Ser Pro Pro Ser Lys Ser His His Lys Lys Ile Val Asn Arg
260 265 270

Asp Val Lys Pro Phe Pro Gly Thr Val Ala Lys Met Phe Leu Ser Thr
275 280 285

Leu Thr Ile Glu Ser Val Thr Lys Ser Asp Gln Gly Glu Tyr Thr Cys
290 295 300

Val Ala Ser Ser Gly Arg Met Ile Lys Arg Asn Arg Thr Phe Val Arg
305 310 315 320

Val His Thr Lys Pro Phe Ile Ala Phe Gly Ser Gly Met Lys Ser Leu
325 330 335

Val Glu Ala Thr Val Gly Ser Gln Val Arg Ile Pro Val Lys Tyr Leu
340 345 350

Ser Tyr Pro Ala Pro Asp Ile Lys Trp Tyr Arg Asn Gly Arg Pro Ile
355 360 365

Glu Ser Asn Tyr Thr Met Ile Val Gly Asp Glu Leu Thr Ile Met Glu
370 375 380

Val Thr Glu Arg Asp Ala Gly Asn Tyr Thr Val Ile Leu Thr Asn Pro
385 390 395 400

Ile Ser Met Glu Lys Gln Ser His Met Val Ser Leu Val Val Asn Val
405 410 415

Pro Pro Gln Ile Gly Glu Lys Ala Leu Ile Ser Pro Met Asp Ser Tyr
420 425 430

Gln Tyr Gly Thr Met Gln Thr Leu Thr Cys Thr Val Tyr Ala Asn Pro
435 440 445

Pro Leu His His Ile Gln Trp Tyr Trp Gln Leu Glu Glu Ala Cys Ser
450 455 460

Tyr Arg Pro Gly Gln Thr Ser Pro Tyr Ala Cys Lys Glu Trp Arg His
465 470 475 480

Val Glu Asp Phe Gln Gly Gly Asn Lys Ile Glu Val Thr Lys Asn Gln
485 490 495

Tyr Ala Leu Ile Glu Gly Lys Asn Lys Thr Val Ser Thr Leu Val Ile
500 505 510

Gln Ala Ala Asn Val Ser Ala Leu Tyr Lys Cys Glu Ala Ile Asn Lys
515 520 525

Ala Gly Arg Gly Glu Arg Val Ile Ser Phe His Val Ile Arg Gly Pro
530 535 540

Glu Ile Thr Val Gln Pro Ala Ala Gln Pro Thr Glu Gln Glu Ser Val
545 550 555 560

Ser Leu Leu Cys Thr Ala Asp Arg Asn Thr Phe Glu Asn Leu Thr Trp
565 570 575

Tyr Lys Leu Gly Ser Gln Ala Thr Ser Val His Met Gly Glu Ser Leu
580 585 590

Thr Pro Val Cys Lys Asn Leu Asp Ala Leu Trp Lys Leu Asn Gly Thr
595 600 605

Met Phe Ser Asn Ser Thr Asn Asp Ile Leu Ile Val Ala Phe Gln Asn
610 615 620

Ala Ser Leu Gln Asp Gln Gly Asp Tyr Val Cys Ser Ala Gln Asp Lys
625 630 635 640

Lys Thr Lys Lys Arg His Cys Leu Val Lys Gln Leu Ile Ile Leu Glu
645 650 655

Arg Met Ala Pro Met Ile Thr Gly Asn Leu Glu Asn Gln Thr Thr Thr
660 665 670

Ile Gly Glu Thr Ile Glu Val Thr Cys Pro Ala Ser Gly Asn Pro Thr
675 680 685

Pro His Ile Thr Trp Phe Lys Asp Asn Glu Thr Leu Val Glu Asp Ser
690 695 700

Gly Ile Val Leu Arg Asp Gly Asn Arg Asn Leu Thr Ile Arg Arg Val
705 710 715 720

Arg Lys Glu Asp Gly Gly Leu Tyr Thr Cys Gln Ala Cys Asn Val Leu
725 730 735

Gly Cys Ala Arg Ala Glu Thr Leu Phe Ile Ile Glu Gly Ala Gln Glu
740 745 750

Lys Thr Asn Leu Glu Val Ile Ile Leu Val Gly Thr Ala Val Ile Ala
755 760 765

Met Phe Phe Trp Leu Leu Leu Val Ile Val Leu Arg Thr Val Lys Arg
770 775 780

Ala Asn Glu Gly Glu Leu Lys Thr Gly Tyr Leu Ser Ile Val Met Asp
785 790 795 800

Pro Asp Glu Leu Pro Leu Asp Glu Arg Cys Glu Arg Leu Pro Tyr Asp
805 810 815

Ala Ser Lys Trp Glu Phe Pro Arg Asp Arg Leu Lys Leu Gly Lys Pro
820 825 830

Leu Gly Arg Gly Ala Phe Gly Gln Val Ile Glu Ala Asp Ala Phe Gly
835 840 845

Ile Asp Lys Thr Ala Thr Cys Lys Thr Val Ala Val Lys Met Leu Lys
850 855 860

Glu Gly Ala Thr His Ser Glu His Arg Ala Leu Met Ser Glu Leu Lys
865 870 875 880

Ile Leu Ile His Ile Gly His His Leu Asn Val Val Asn Leu Leu Gly
885 890 895

Ala Cys Thr Lys Pro Gly Gly Pro Leu Met Val Ile Val Glu Phe Cys
900 905 910

Lys Phe Gly Asn Leu Ser Thr Tyr Leu Arg Gly Lys Arg Asn Glu Phe
915 920 925

Val Pro Tyr Lys Ser Lys Gly Ala Arg Phe Arg Gln Gly Lys Asp Tyr
930 935 940

Val Gly Glu Leu Ser Val Asp Leu Lys Arg Arg Leu Asp Ser Ile Thr
945 950 955 960

Ser Ser Gln Ser Ser Ala Ser Ser Gly Phe Val Glu Glu Lys Ser Leu
965 970 975

Ser Asp Val Glu Glu Glu Glu Ala Ser Glu Glu Leu Tyr Lys Asp Phe
980 985 990

Leu Thr Leu Glu His Leu Ile Cys Tyr Ser Phe Gln Val Ala Lys Gly
995 1000 1005

Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala
1010 1015 1020

Ala Arg Asn Ile Leu Leu Ser Glu Lys Asn Val Val Lys Ile Cys
1025 1030 1035

Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val
1040 1045 1050

Arg Lys Gly Asp Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu
1055 1060 1065

Thr Ile Phe Asp Arg Val Tyr Thr Ile Gln Ser Asp Val Trp Ser
1070 1075 1080

Phe Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro
1085 1090 1095

Tyr Pro Gly Val Lys Ile Asp Glu Glu Phe Cys Arg Arg Leu Lys
1100 1105 1110

Glu Gly Thr Arg Met Arg Ala Pro Asp Tyr Thr Thr Pro Glu Met
1115 1120 1125

Tyr Gln Thr Met Leu Asp Cys Trp His Glu Asp Pro Asn Gln Arg
1130 1135 1140

Pro Ser Phe Ser Glu Leu Val Glu His Leu Gly Asn Leu Leu Gln
1145 1150 1155

Ala Asn Ala Gln Gln Asp Gly Lys Asp Tyr Ile Val Leu Pro Met
1160 1165 1170

Ser Glu Thr Leu Ser Met Glu Glu Asp Ser Gly Leu Ser Leu Pro
1175 1180 1185

Thr Ser Pro Val Ser Cys Met Glu Glu Glu Glu Val Cys Asp Pro
1190 1195 1200

Lys Phe His Tyr Asp Asn Thr Ala Gly Ile Ser His Tyr Leu Gln
1205 1210 1215

Asn Ser Lys Arg Lys Ser Arg Pro Val Ser Val Lys Thr Phe Glu
1220 1225 1230

Asp Ile Pro Leu Glu Glu Pro Glu Val Lys Val Ile Pro Asp Asp
1235 1240 1245

Ser Gln Thr Asp Ser Gly Met Val Leu Ala Ser Glu Glu Leu Lys
1250 1255 1260

Thr Leu Glu Asp Arg Asn Lys Leu Ser Pro Ser Phe Gly Gly Met
1265 1270 1275

Met Pro Ser Lys Ser Arg Glu Ser Val Ala Ser Glu Gly Ser Asn
1280 1285 1290

Gln Thr Ser Gly Tyr Gln Ser Gly Tyr His Ser Asp Asp Thr Asp
1295 1300 1305

Thr Thr Val Tyr Ser Ser Asp Glu Ala Gly Leu Leu Lys Met Val
1310 1315 1320

Asp Ala Ala Val His Ala Asp Ser Gly Thr Thr Leu Arg Ser Pro
1325 1330 1335

Pro Val
1340