SEQUENCE LISTING

<110> ESBATech AG

<120> Stable and soluble antibodies inhibiting TNFalpha

<130> 12013PC

<160> 40

<170> PatentIn version 3.3

<210> 1
<211> 108
<212> PRT
<213> artificial

<220>
<223> derivative of TB-B

<220>
<221> VL/TB-A
<222> (1)..(108)

<400> 1

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg
100 105

<210> 2
<211> 117
<212> PRT
<213> artificial

<220>
<223> derivative of TB-B

<220>
<221> VH/TB-A
<222> (1)..(117)

<400> 2

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

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
            20                  25                  30

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

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
    50                  55                  60

Lys Asp Arg Phe Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
65                  70                  75                  80

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser
        115
```

<210> 3
<211> 108
<212> PRT
<213> human-murine

<220>
<221> VL/TB-B
<222> (1)..(108)

<400> 3

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95
```

```
Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg
            100                 105


<210>  4
<211>  117
<212>  PRT
<213>  human-murine


<220>
<221>  VH/TB-B
<222>  (1)..(117)

<400>  4

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


Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Ser Phe Thr His Tyr
            20                  25                  30


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


Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
    50                  55                  60


Lys Asp Arg Val Thr Leu Thr Arg Asp Thr Ser Ile Gly Thr Val Tyr
65                  70                  75                  80


Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110


Val Thr Val Ser Ser
        115


<210>  5
<211>  108
<212>  PRT
<213>  human


<220>
<221>  VL/FW2.3
<222>  (1)..(108)

<400>  5

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


Asp Arg Val Thr Leu Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Glu
            20                  25                  30
```

```
Leu Ala Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45

Tyr Ala Gly Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Leu Pro Tyr
                85                  90                  95

Met Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg
            100                 105
```

<210> 6
<211> 124
<212> PRT
<213> human

<220>
<221> VH/FW2.3
<222> (1)..(124)

<400> 6

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
            20                  25                  30

Phe Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asn Pro Asp Ser Gly Asp Thr Ile Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Asp Arg Val Thr Leu Thr Arg Asp Thr Ser Ile Gly Thr Val Tyr
65                  70                  75                  80

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Val Pro Arg Gly Thr Tyr Leu Asp Pro Trp Asp Tyr Phe Asp
            100                 105                 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 7
<211> 108

<212> PRT
<213> artificial

<220>
<223> derivative of TB-A

<220>
<221> VL/TB_L2
<222> (1)..(108)

<400> 7

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Gly Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg
100 105

<210> 8
<211> 108
<212> PRT
<213> artificial

<220>
<223> derived from TB-A

<220>
<221> VL/TB_L3
<222> (1)..(108)

<400> 8

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Leu Pro Tyr
85 90 95

Met Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg
100 105

<210> 9
<211> 117
<212> PRT
<213> artificial

<220>
<223> derivative of TB-A

<220>
<221> VH/TB_H2
<222> (1)..(117)

<400> 9

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

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

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

Gly Arg Ile Asn Pro Asp Ser Gly Asp Thr Ile Tyr Ala Gln Lys Phe
50 55 60

Gln Asp Arg Phe Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 10
<211> 20
<212> PRT
<213> artificial linker

<220>
<223> artificial linker sequence

<220>
<221> Glycine-Serine Linker
<222> (1)..(20)

<400> 10

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 11
<211> 108
<212> PRT
<213> artificial

<220>
<223> derivative of TB-B

<220>
<221> VL/TB-B R46L
<222> (1)..(108)

<400> 11

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg
100 105

<210> 12
<211> 245
<212> PRT
<213> artificial

<220>
<223> scFV , human-murine with artificial linker

<220>
<221> TB-AB
<222> (1)..(245)
<223> VL(TB-A)-linker-VH(TB-B)

<400> 12

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
100 105 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
130 135 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Ser Phe Thr His Tyr
145 150 155 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
165 170 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
180 185 190

Lys Asp Arg Val Thr Leu Thr Arg Asp Thr Ser Ile Gly Thr Val Tyr
195 200 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
210 215 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225 230 235 240

Val Thr Val Ser Ser
245

<210> 13
<211> 245
<212> PRT
<213> artificial

<220>
<223> scFv, human-murine with artificial linker

<220>
<221> TB-BA
<222> (1)..(245)
<223> VL(TB-B)-linker-VH(TB-A)

<400> 13

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
100 105 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
130 135 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145 150 155 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
165 170 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
180 185 190

```
Lys Asp Arg Phe Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 14
<211> 106
<212> PRT
<213> human

<220>
<221> C-kappa of human Ig
<222> (1)..(105)

<400> 14

```
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1               5                   10                  15

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

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
        35                  40                  45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
    50                  55                  60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65                  70                  75                  80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
                85                  90                  95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
            100                 105
```

<210> 15
<211> 105
<212> PRT
<213> human

<220>
<221> CH1 of human IgG
<222> (1)..(105)

<400> 15

```
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 Ser 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 Thr Ser
            100                 105
```

<210> 16
<211> 108
<212> PRT
<213> murine

<220>
<221> VL/TBwt
<222> (1)..(108)

<400> 16

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

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

Val Val Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Met Leu Met
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
    50                  55                  60

Arg Gly Tyr Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Val Gln Ala
65                  70                  75                  80

Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

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

<210> 17
<211> 117
<212> PRT
<213> murine

<220>
<221> VH/TBwt
<222> (1)..(117)

<400> 17

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

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

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

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Glu His Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Phe
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser
115

<210> 18
<211> 245
<212> PRT
<213> artificial

<220>
<223> scFV, human-murine with artificial linker

<220>
<221> TB-A H43
<222> (1)..(245)
<223> scFv VL(TB-A)-linker-VH(TB-A K43Q)

<400> 18

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
100 105 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
130 135 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145 150 155 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
165 170 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
180 185 190

Lys Asp Arg Phe Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
195 200 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
210 215 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225 230 235 240

Val Thr Val Ser Ser
245

<210> 19
<211> 245
<212> PRT
<213> artificial

<220>
<223> scFv, human-murine with artificial linker

<220>
<221> TB-A H70/72

<222> (1)..(245)
<223> scFv VL(TB-A)-linker-VH(TB-A F70L/L72R)

<400> 19

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
    130                 135                 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145                 150                 155                 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Val Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 20
<211> 245
<212> PRT
<213> artificial

<220>
<223> scFv, human-murine with artificial linker

<220>
<221> TB-A H70/72
<222> (1)..(245)
<223> scFv VL(TB-A)-linker-VH(TB-A F70L/L72R)

<400> 20

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
    130                 135                 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145                 150                 155                 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Phe Thr Leu Ser Arg Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205
```

```
Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 21
<211> 245
<212> PRT
<213> artificial

<220>
<223> scFv, human-murine with artificial linker

<220>
<221> TB-A H76/77
<222> (1)..(245)
<223> scFv VL(TB-A)-linker-VH(TB-A A76I/S77G)

<400> 21

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
    130                 135                 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145                 150                 155                 160
```

```
Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Phe Thr Phe Ser Leu Glu Thr Ser Ile Gly Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 22
<211> 245
<212> PRT
<213> artificial

<220>
<223> scFv, human-murine with artificial linker

<220>
<221> TB-A L46
<222> (1)..(245)
<223> scFv VL(TB-A L46R)-linker-VH(TB-A)

<400> 22

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110
```

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
130 135 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145 150 155 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
165 170 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
180 185 190

Lys Asp Arg Phe Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
195 200 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
210 215 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225 230 235 240

Val Thr Val Ser Ser
245

<210> 23
<211> 245
<212> PRT
<213> artificial

<220>
<223> scFv, human-murine with artificial linker

<220>
<221> TB-A L65
<222> (1)..(245)
<223> scFv VH(TB-A R65S)-linker-VH(TB-A)

<400> 23

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
    130                 135                 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145                 150                 155                 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Phe Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 24
<211> 245
<212> PRT
<213> artificial

<220>
<223> scFv, human-murine with artificial linker

<220>
<221> TB-A L67
<222> (1)..(245)
<223> scFv VL(TB-A Y67S)-linker-VH(TB-A)

<400> 24

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

```
Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
    130                 135                 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145                 150                 155                 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Phe Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 25
<211> 117
<212> PRT
<213> artificial

<220>
<223> derived from TB-A

<220>
<221> VH/TB-A D66G
<222> (1)..(117)

<400> 25

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

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

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

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Lys Gly Arg Phe Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 26
<211> 108
<212> PRT
<213> artificial

<220>
<223> drived from TB-A

<220>
<221> VL/TB-A V83F
<222> (1)..(108)

<400> 26

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly

50 55 60

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

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg
100 105

<210> 27
<211> 108
<212> PRT
<213> artificial

<220>
<223> derived from TB-A

<220>
<221> VL/TB-A V83A
<222> (1)..(108)

<400> 27

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Ala Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg
100 105

<210> 28
<211> 117
<212> PRT
<213> artificial

<220>
<223> derived from TB-A

<220>

<221> VH/TB-AH43/70/71/73/77
<222> (1)..(117)
<223> VH of TB-A with K43Q/F70L/S71T/E73D/S77G

<220>
<221> VH/TB-A H43/70/71/73/77
<222> (1)..(117)
<223> VH of TB-A with K43Q/F70L/S71T/E73D/S77G

<400> 28

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
            20                  25                  30

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

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
    50                  55                  60

Lys Asp Arg Phe Thr Leu Thr Leu Asp Thr Ser Ala Gly Thr Val Tyr
65                  70                  75                  80

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser
        115
```

<210> 29
<211> 117
<212> PRT
<213> artificial

<220>
<223> derived from TB-A

<220>
<221> VH/TB-A H43/70/71
<222> (1)..(117)
<223> VH of TB-A with K43Q/F70L/S71T

<400> 29

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
            20                  25                  30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
```

35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Lys Asp Arg Phe Thr Leu Thr Leu Glu Thr Ser Ala Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 30
<211> 117
<212> PRT
<213> artificial

<220>
<223> derived from TB-A

<220>
<221> VH/TB-A H11/16/43/66/70/73/77/93/112
<222> (1)..(117)
<223> VH of TB-A with V11D/A16GK43Q/D66G/F70L/S71T/E73D/S77G/V93T/L112S

<220>
<221> VH/TB-A H11/16/43/66/70/73/77/93/112
<222> (1)..(117)
<223> VH of TB-A with
V11D/A16G/K43Q/D66G/F70L/S71T/E73D/S77G/V93T/L112S

<400> 30

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Asp Lys Lys Pro Gly Gly
1 5 10 15

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

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

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Lys Gly Arg Phe Thr Leu Thr Leu Asp Thr Ser Ala Gly Thr Val Tyr
65 70 75 80

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser
115

<210> 31
<211> 245
<212> PRT
<213> artificial

<220>
<223> Derivative of TB-A

<220>
<221> TB-A H_M48L/F68I
<222> (1)..(245)
<223> TB-A with VL of TB-A and VH M48L and F68I linked by SEQ ID NO:10

<400> 31

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
100 105 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
130 135 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145 150 155 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
165 170 175

```
Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Ile Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 32
<211> 245
<212> PRT
<213> artificial

<220>
<223> Derivative of TB-A

<220>
<221> TB-A L_V83E H_V79A
<222> (1)..(245)
<223> TB-A with VL V83E and VH_V79A linked by SEQ ID NO: 10

<400> 32

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Glu Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125
```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
130 135 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145 150 155 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
165 170 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
180 185 190

Lys Asp Arg Phe Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
195 200 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
210 215 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225 230 235 240

Val Thr Val Ser Ser
245

<210> 33
<211> 245
<212> PRT
<213> artificial

<220>
<223> Derivative of TB-A

<220>
<221> TB-A Linker_G2R H_F68L
<222> (1)..(245)
<223> TB-A with VL of TB-A and VH_F68L linked by SEQ ID NO:39

<400> 33

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

```
Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Arg Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
    130                 135                 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145                 150                 155                 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Leu Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 34
<211> 245
<212> PRT
<213> artificial

<220>
<223> Derivative of TB-A

<220>
<221> TB-A H_K43R/F68I
<222> (1)..(245)
<223> TB-A with VL of TB-A and VH_K34R_F68I linked by SEQ ID NO:10

<400> 34

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30
```

```
Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
    130                 135                 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145                 150                 155                 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Ile Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 35
<211> 245
<212> PRT
<213> artificial

<220>
<223> Derivative of TB-A

<220>
<221> TB-A H_F68L

<222> (1)..(245)
<223> TB-A with VL of TB-A and VH_F68L linked by SEQ ID NO:10

<400> 35

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
    130                 135                 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145                 150                 155                 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Leu Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 36
<211> 245
<212> PRT
<213> artificial

<220>
<223> Derivative of TB-A

<220>
<221> TB-A H_F68A
<222> (1)..(245)
<223> TB-A with VL of TB-A and VH_F68A linked by SEQ ID NO:10

<400> 36

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
    130                 135                 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145                 150                 155                 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Ala Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205
```

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
210 215 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225 230 235 240

Val Thr Val Ser Ser
245

<210> 37
<211> 245
<212> PRT
<213> artificial

<220>
<223> Derivative of TB-A

<220>
<221> TB-A H_F68V/F70L
<222> (1)..(245)
<223> TB-A with VL of TB-A and VH_F68V/F70L linked by SEQ ID NO:10

<400> 37

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
100 105 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
130 135 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145 150 155 160

```
Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Val Thr Leu Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240

Val Thr Val Ser Ser
                245
```

<210> 38
<211> 245
<212> PRT
<213> artificial

<220>
<223> Derivative of TB-A

<220>
<221> TB-A H_F70L
<222> (1)..(245)
<223> TB-A with VL of TB-A and VH_F70L linked by SEQ ID NO:10

<400> 38

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110
```

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
130 135 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145 150 155 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
165 170 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
180 185 190

Lys Asp Arg Phe Thr Leu Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
195 200 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
210 215 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225 230 235 240

Val Thr Val Ser Ser
245

<210> 39
<211> 20
<212> PRT
<213> artificial

<220>
<223> linker

<220>
<221> G2RLinker
<222> (1)..(20)

<400> 39

Gly Arg Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 40
<211> 245
<212> PRT
<213> artificial

<220>
<223> TB-A scFv antibody

<220>
<221> TB-A
<222> (1)..(245)
<223> ESBA105

<400> 40

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

Asp Arg Val Thr Leu Thr Cys Thr Ala Ser Gln Ser Val Ser Asn Asp
            20                  25                  30

Val Val Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Phe Asn Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

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

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Asn Ser Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Val Lys Arg Gly Gly Gly Gly
            100                 105                 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
    130                 135                 140

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr His Tyr
145                 150                 155                 160

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
                165                 170                 175

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
            180                 185                 190

Lys Asp Arg Phe Thr Phe Ser Leu Glu Thr Ser Ala Ser Thr Val Tyr
        195                 200                 205

Met Glu Leu Thr Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
    210                 215                 220

Ala Arg Glu Arg Gly Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225                 230                 235                 240
```

Val Thr Val Ser Ser
245