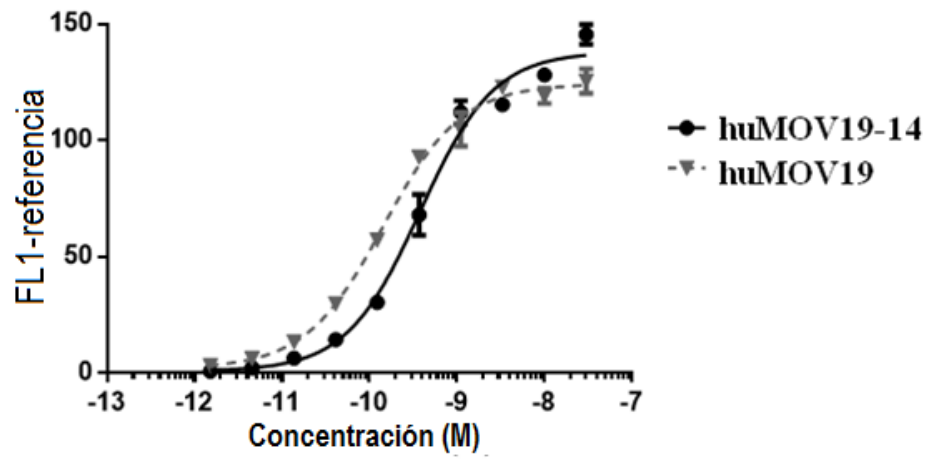


FIG. 1

Afinidad de unión de huMOV19-14 contra el anticuerpo huMOV19 en células T47D



	huMOV19-14	huMOV19
EC50	3.793e-010	1.438e-010

FIG. 2

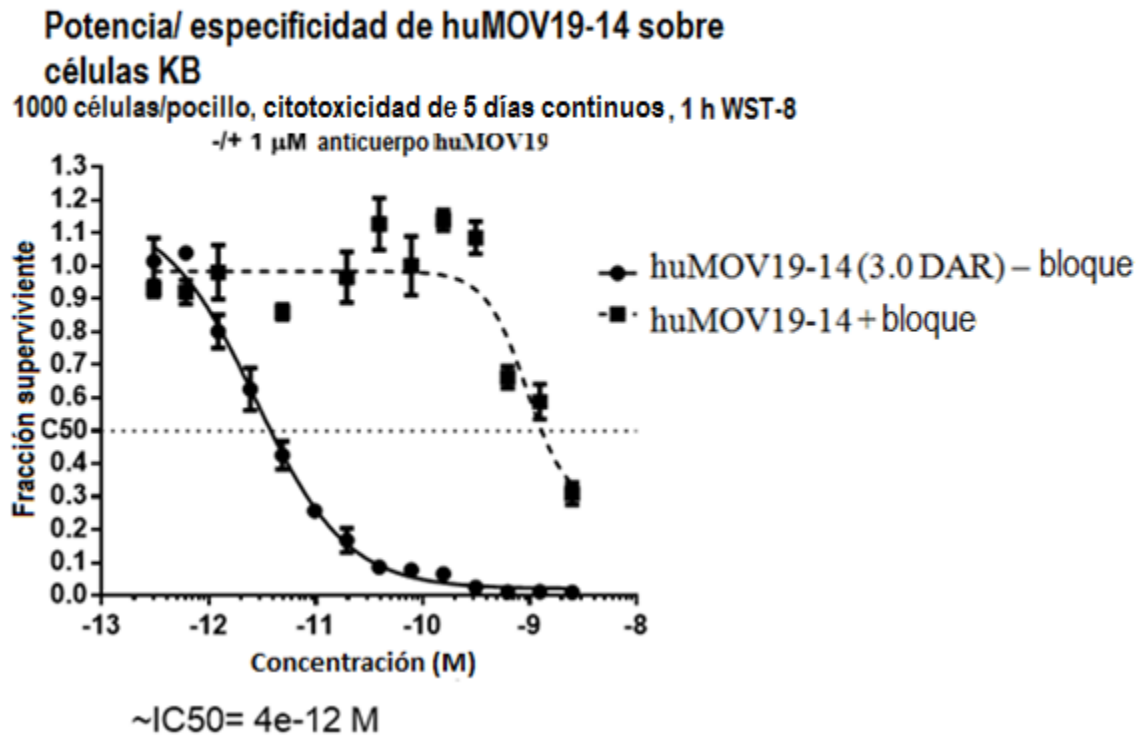


FIG. 3

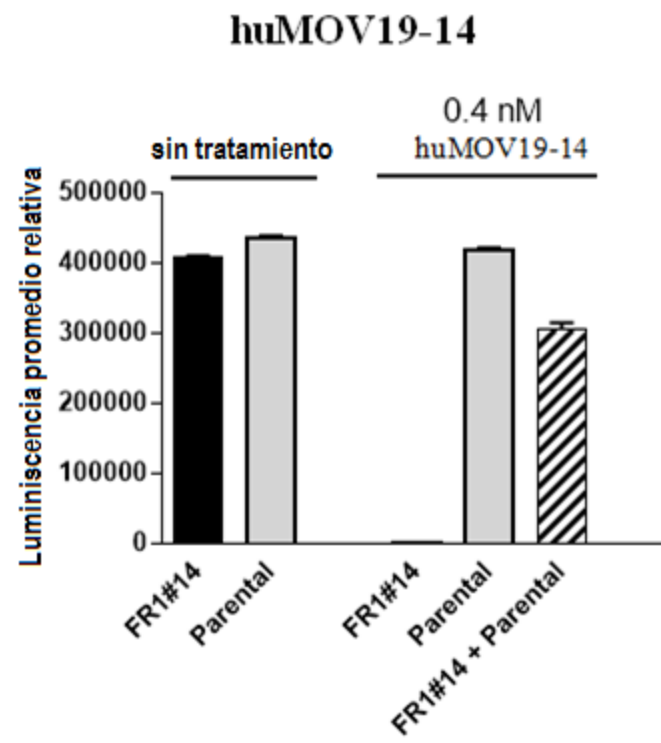


FIG. 4A

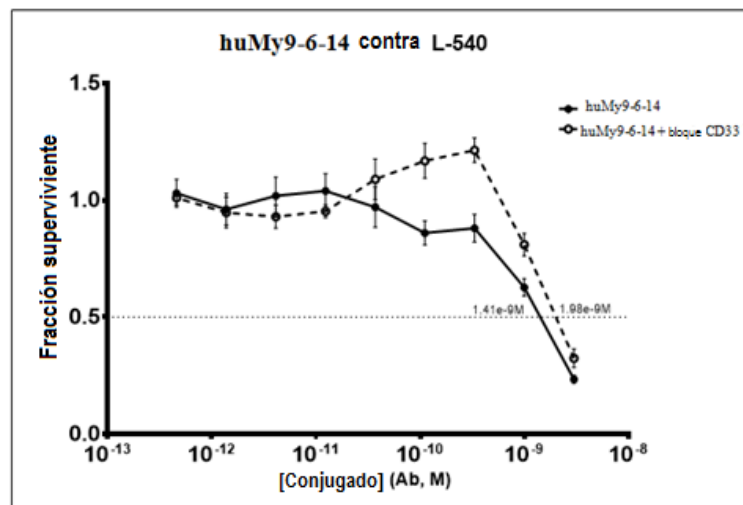
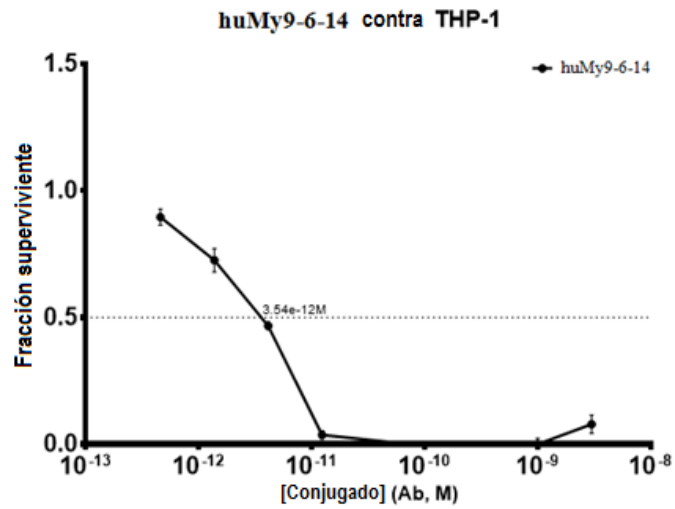


FIG. 4B

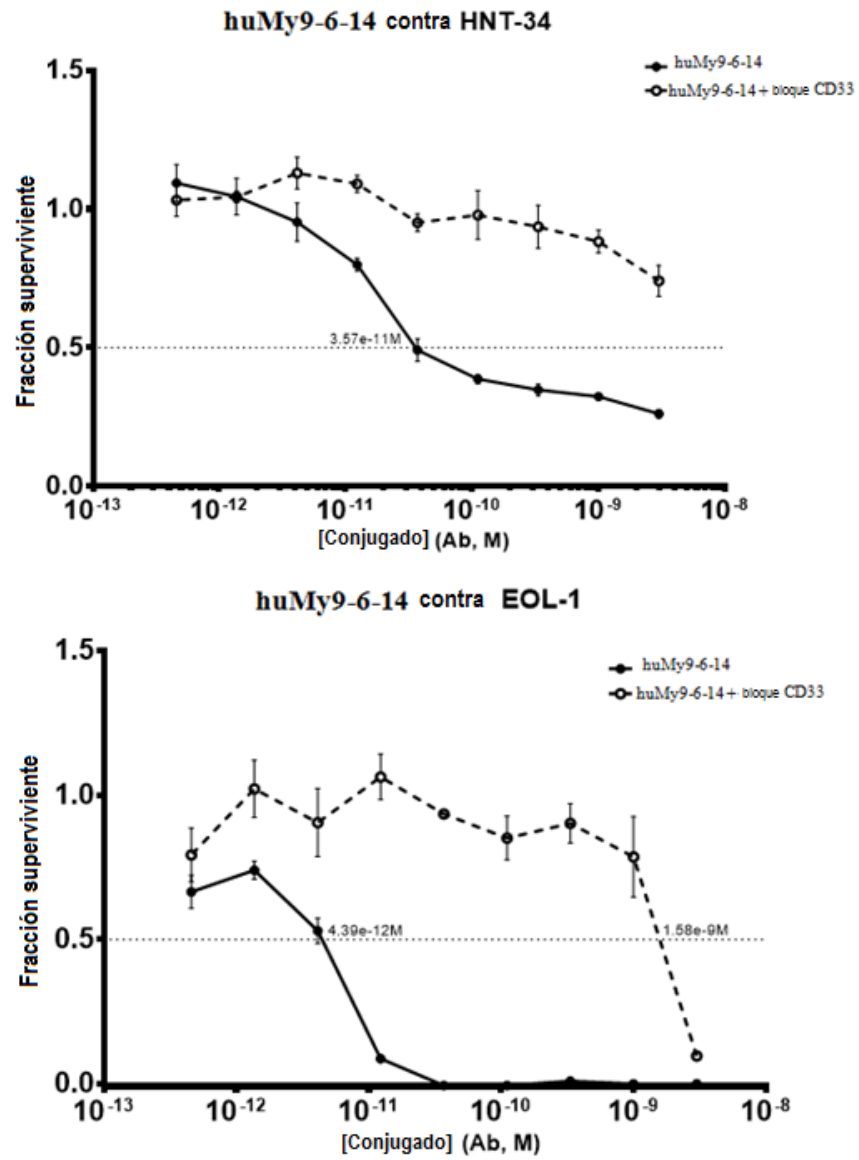


FIG. 4C

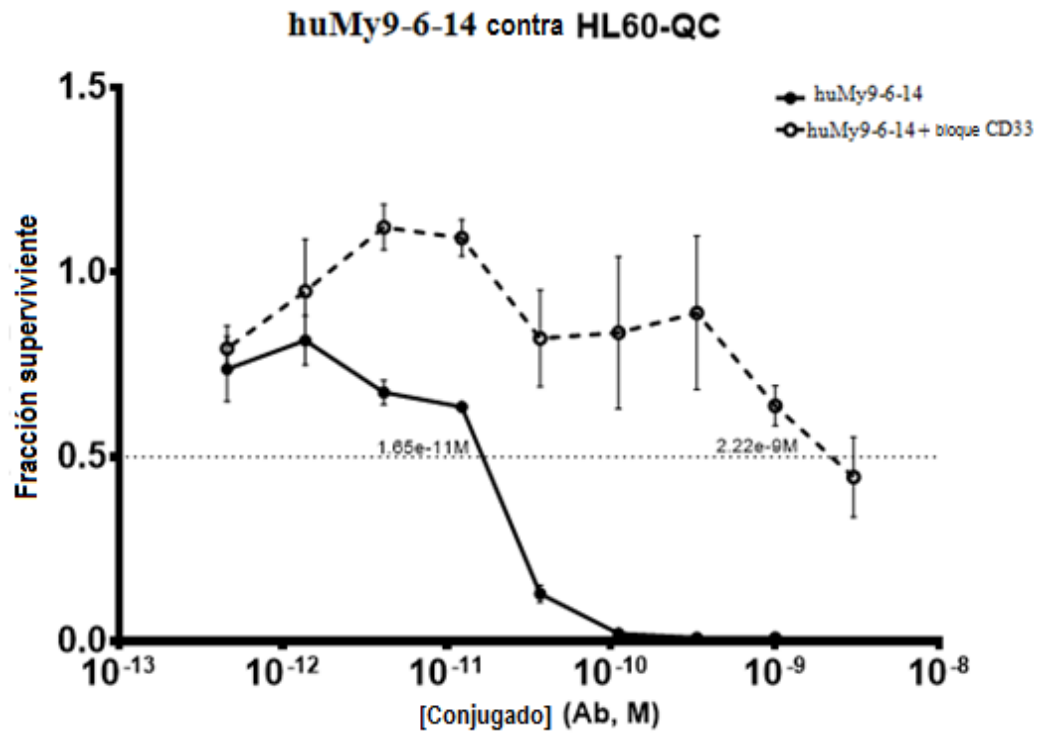


FIG. 5A

Efecto de 0, 500, 1000, 2000 y 4000 células kara (CD33+) sobre 500 células RADA-1 (CD33-) en presencia de conjugado de $1.0 \times 10^{-9} \text{M}$ huMy9-6-14

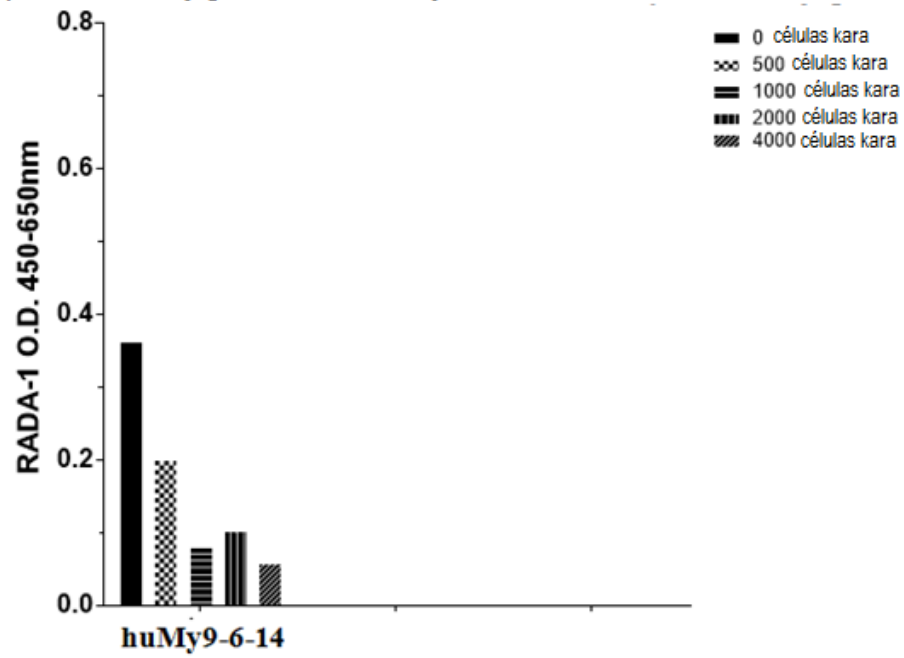


FIG. 5B

Efecto de 0, 500, 1000, 2000 y 4000 células kara (CD33+) sobre 500 células RADA-1 (CD33-) en presencia de conjugado de 5.0×10^{-10} M huMy9-6-14

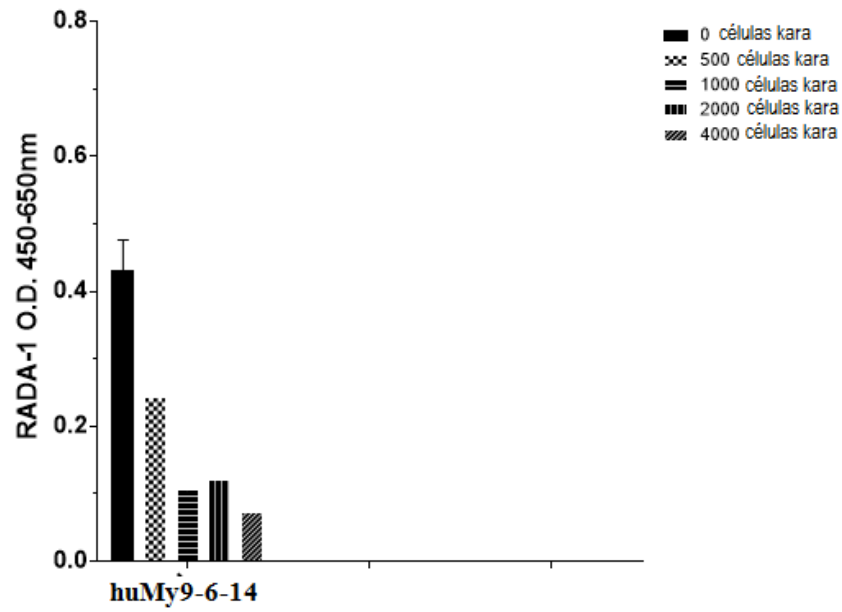
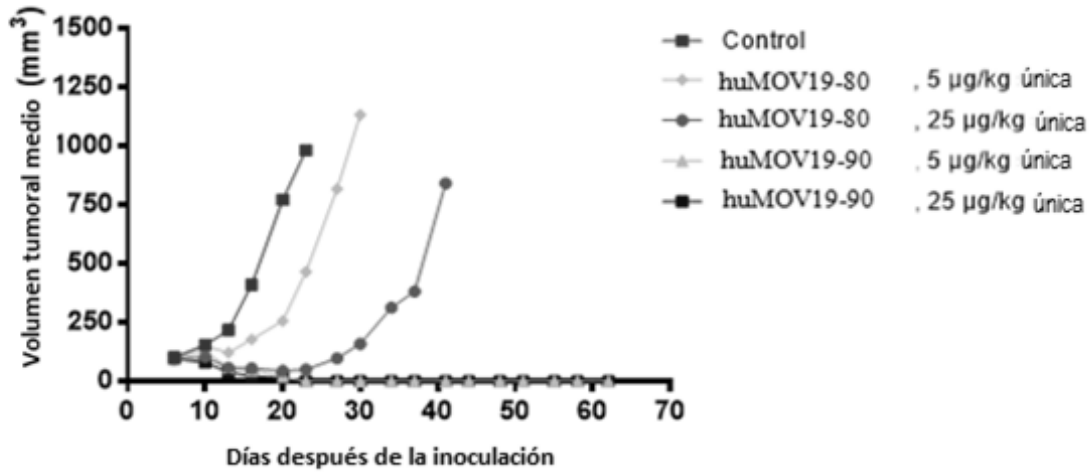


FIG. 6

Actividad antitumoral (volumen tumoral medio, mm³) de huMOV19-80 y huMOV19-90 en ratones SCID que poseen xenoinjertos de NCI-H2110



Grupo de tratamiento		Dosis (ug/kg)	T/C (Día 23)	Regresiones		Resultado
				PR	CR	
A	Control	-	-	-	-	-
B	huMOV19-80	5	47%	0/6	0/6	Inactivo
C	huMOV19-80	25	5%	5/6	1/6	Altamente activo
D	huMOV19-90	5	0%	6/6	6/6	Altamente activo
E	huMOV19-90	25	0%	6/6	6/6	Altamente activo

FIG. 7A

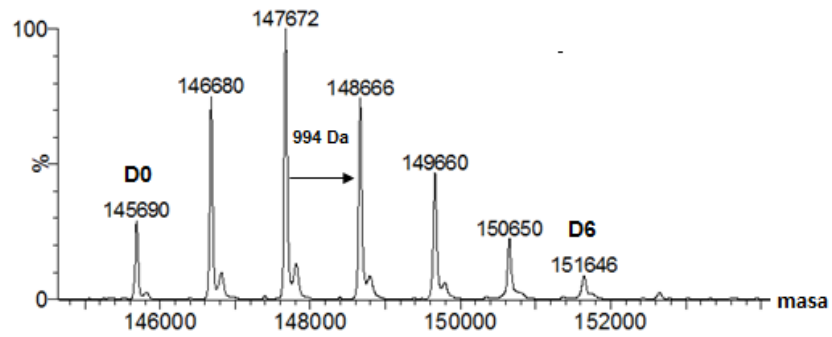
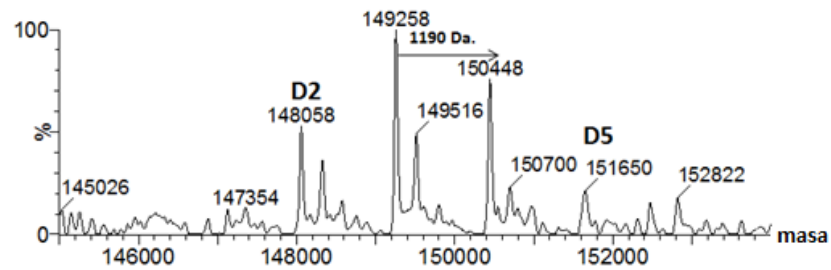
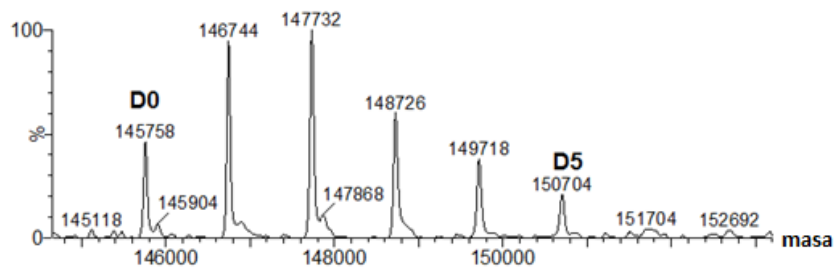
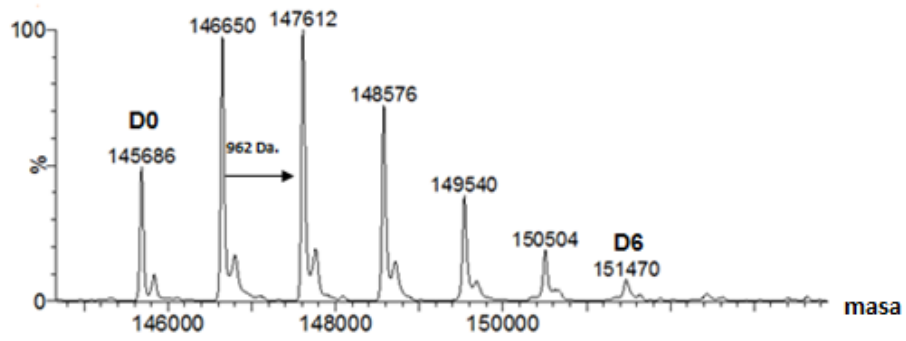
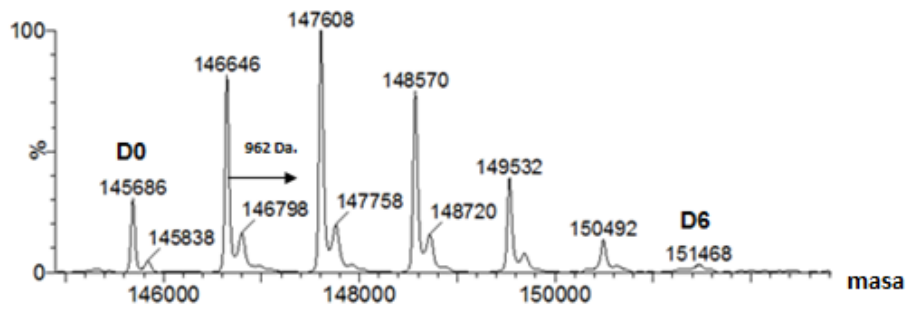
MS para conjugado de huMov19-14 desglucosilado**MS para conjugado de huMov19-sulfo-SPDB-98 desglucosilado****MS para conjugado de huMov19-35 desglucosilado**

FIG. 7B

MS para conjugado de huMov19-63 desglucosilado



MS para conjugado de huMov19-80 desglucosilado



MS para conjugado de huMOV19-90 desglucosilado

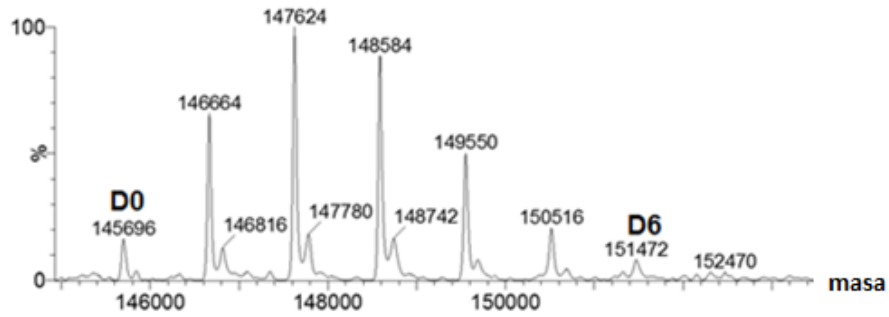
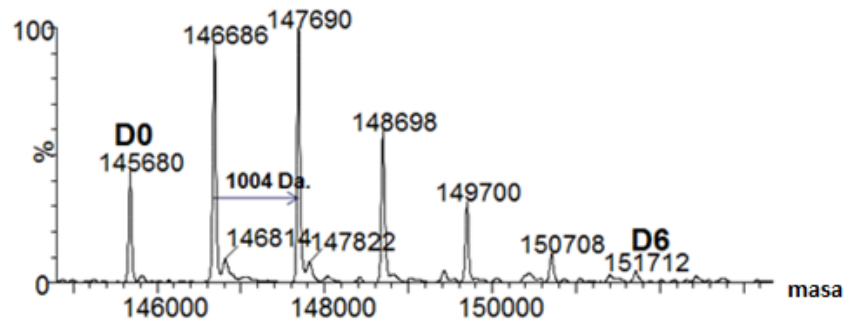
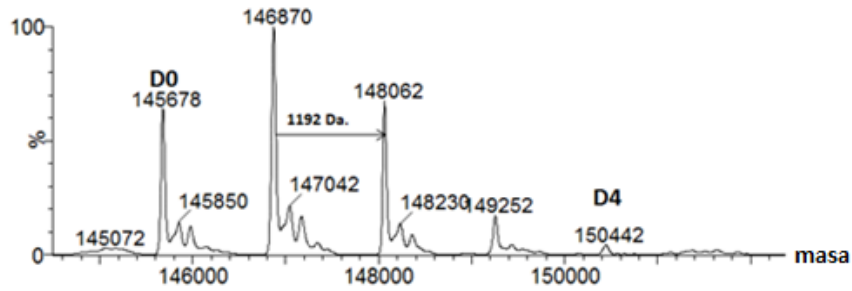


FIG. 7C

MS para conjugado de huMov19-49 desglucosilado



MS para conjugado de huMov19-sulfo-SPDB-99 desglucosilado



MS para conjugado de huMov19-70 desglucosilado

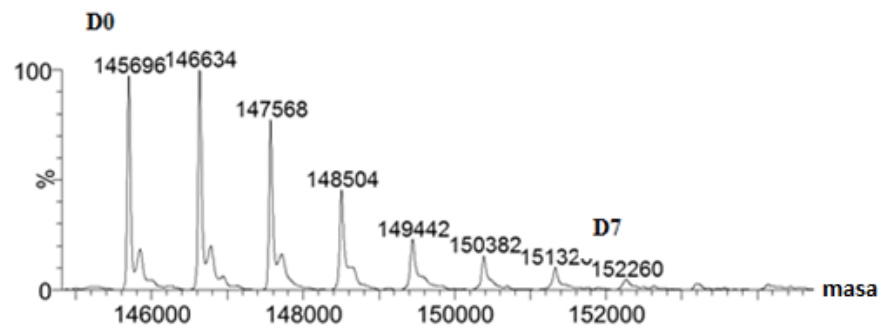


FIG. 7D

MS para conjugado de huMov19-23 desglicosilado

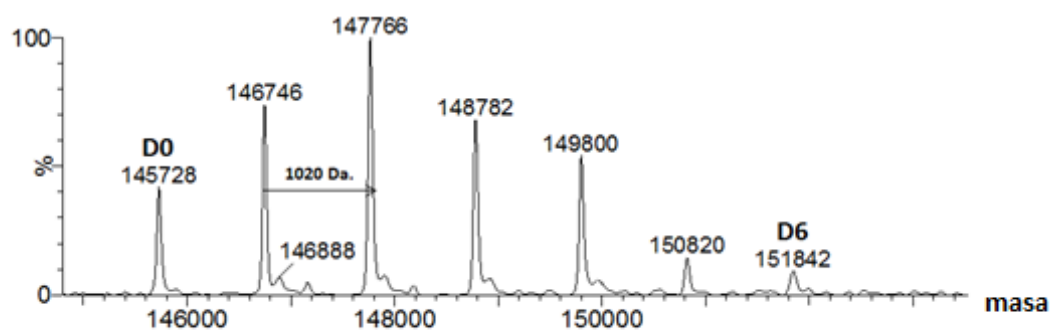


FIG. 8

MS para conjugado de huML66-90 desglucosilado

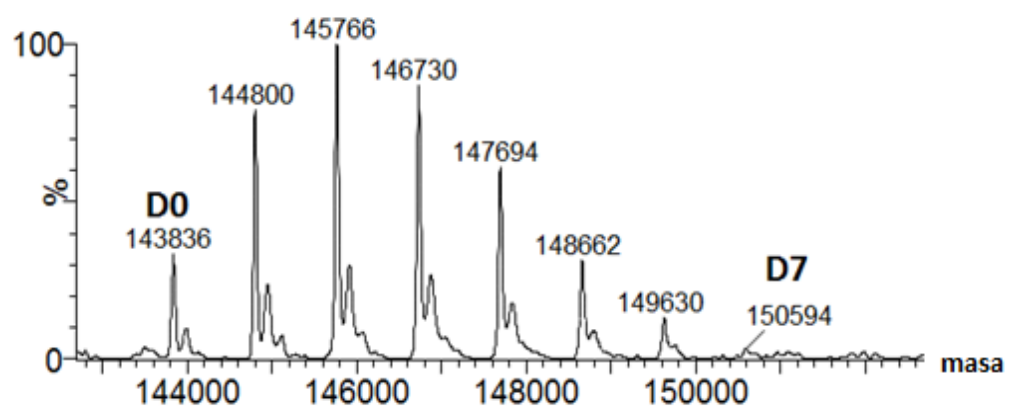


FIG. 9

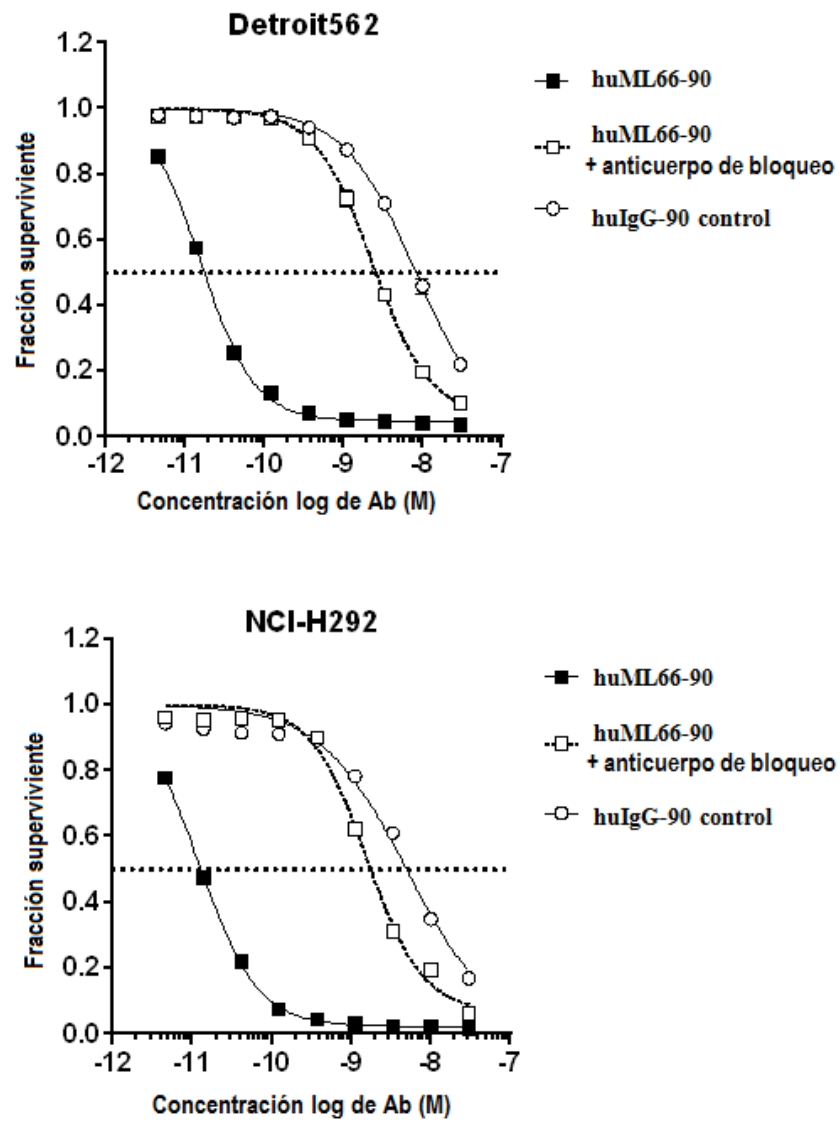


FIG. 10

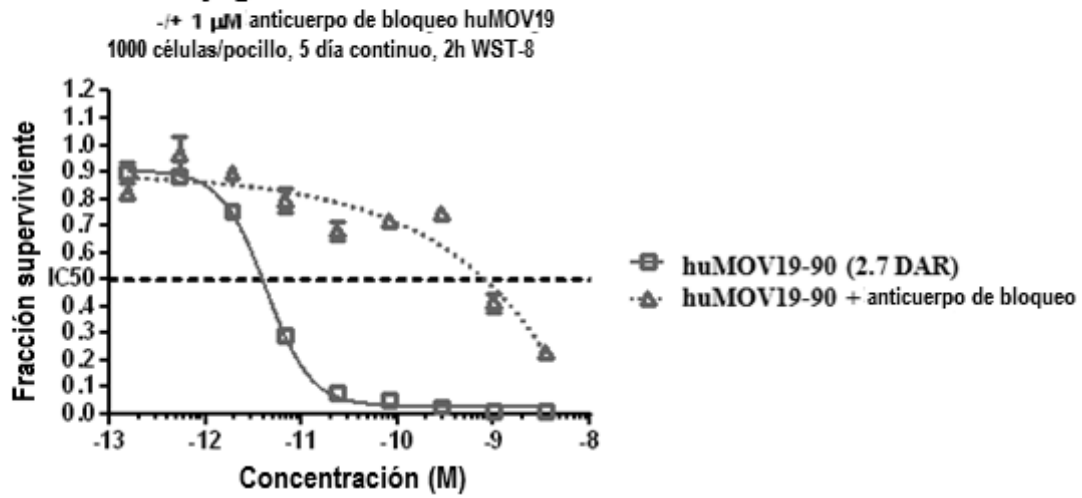
Potencia de conjugado de huMOV19-90 sobre células KB

FIG. 11

Potencia de huMOV19-90 sobre células NCI-H2110

-/+ 1 μ M anticuerpo de bloqueo huMOV19
2000 células/pocillo, 5 día continuo, 3h WST-8

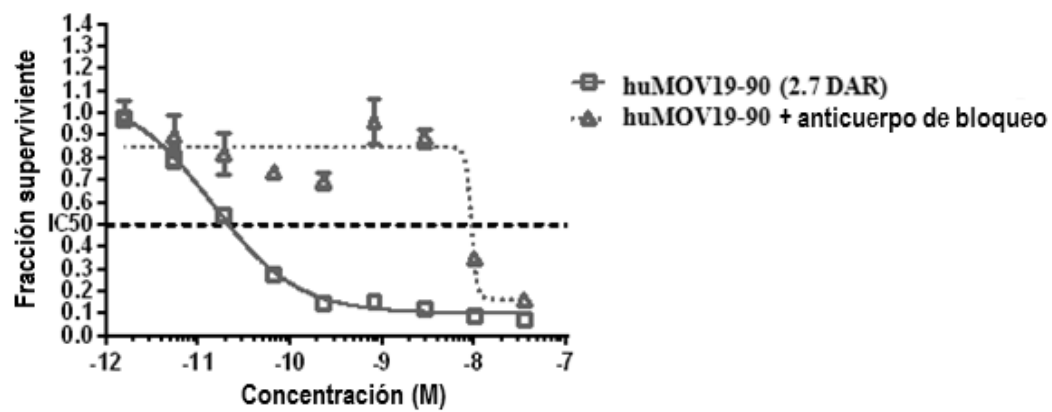


FIG. 12

Potencia de huMOV19-90 sobre células T47D-/+ 1 μ M anticuerpo de bloqueo huMOV19

2000 células/pocillo, 6 día incubación continua, A lamar Blue O/N

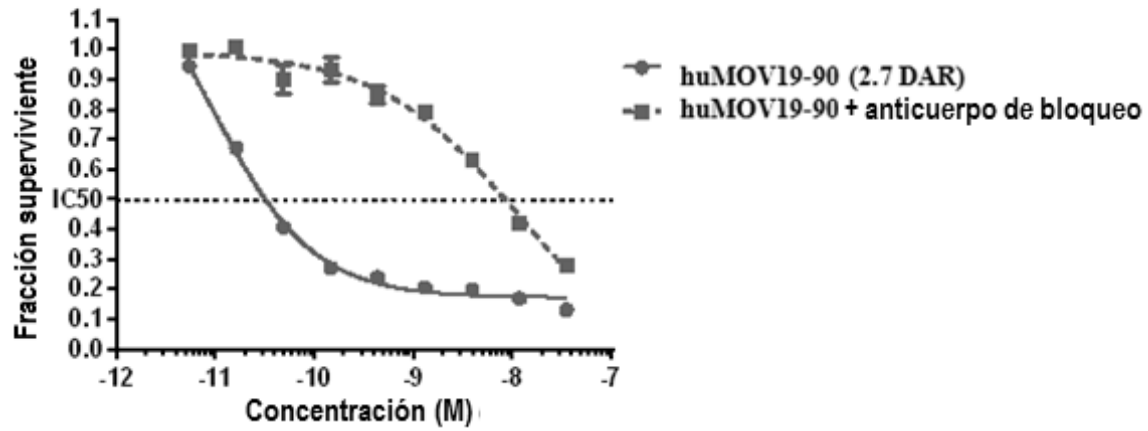


FIG. 13

huMOV19-90

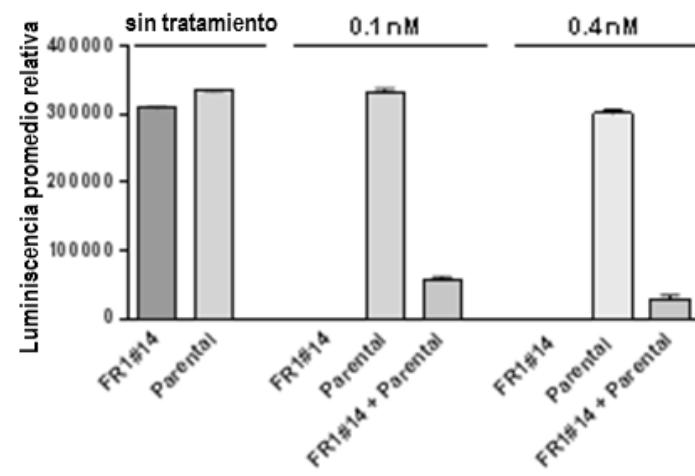
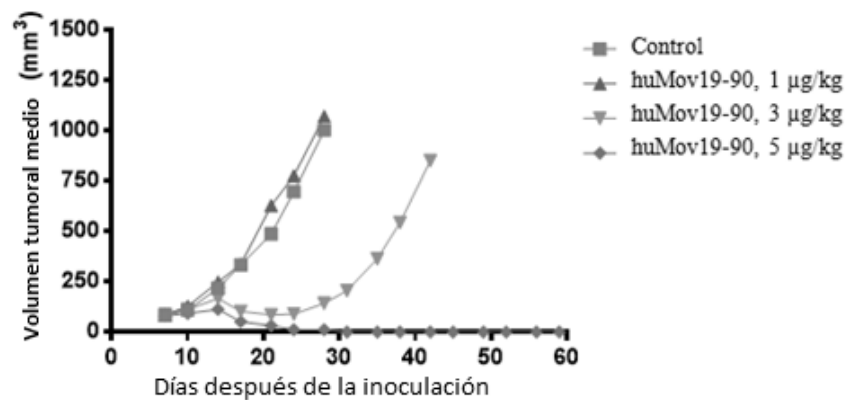


FIG. 14

Actividad antitumoral (volumen tumoral medio, mm³) de huMOV19-90 en ratones SCID que poseen xenoinjertos de NCI-H2110



Grupo de tratamiento		Dosis del compuesto (µg/kg)	T/C (Día 28)	Regresiones		Resultado
				PR	CR	
A	Control	-	-	-	-	-
B	huMov19-90	1	107%	0/6	0/6	Inactivo
C	huMov19-90	3	14%	1/6	0/6	Activo
D	huMov19-90	5	1%	6/6	3/6	Altamente activo

FIG. 15

FIG. 15A

Unión de conjugado de huMOV19-90 sobre células T47D

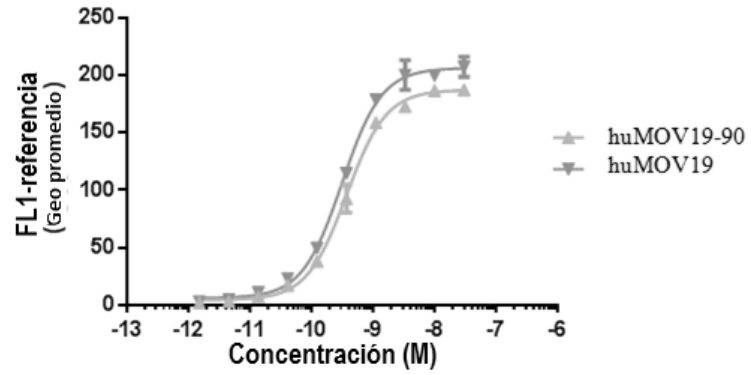


FIG. 15B

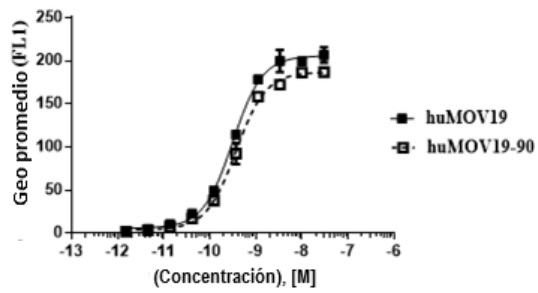


FIG. 16

MS para conjugado de huMov19-sulfo-SPDB-107 desglucosilado

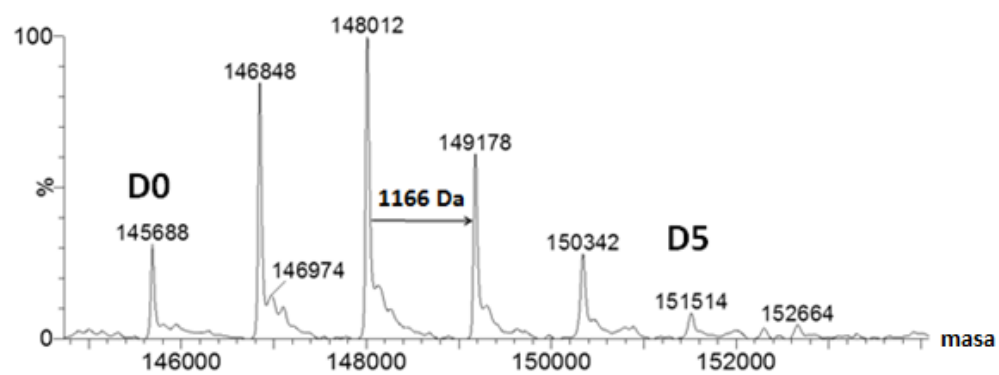
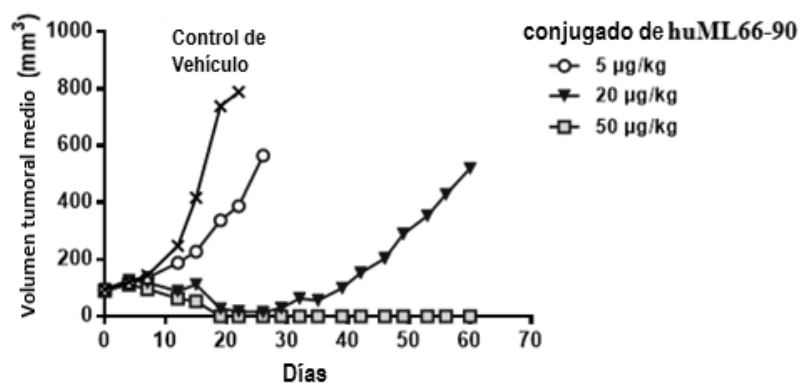


FIG. 17

Actividad antitumoral (volumen tumoral medio, mm³) de conjugado de huML66-90 en ratones SCID que poseen xenoinjertos de NCI-H1703



Agente	Dosis de compuesto 90 (µg/kg)	Dosis de Ab (mg/kg)	T/C (%)	CR	Resultado
conjugado de huML66-90	5	0.3	46	0/6	Inactivo
	20	1.1	4	3/6	Altamente activo
	50	2.8	0	6/6	Altamente activo

FIG. 18

Farmacocinética de huMov19-90 en ratones CD-1

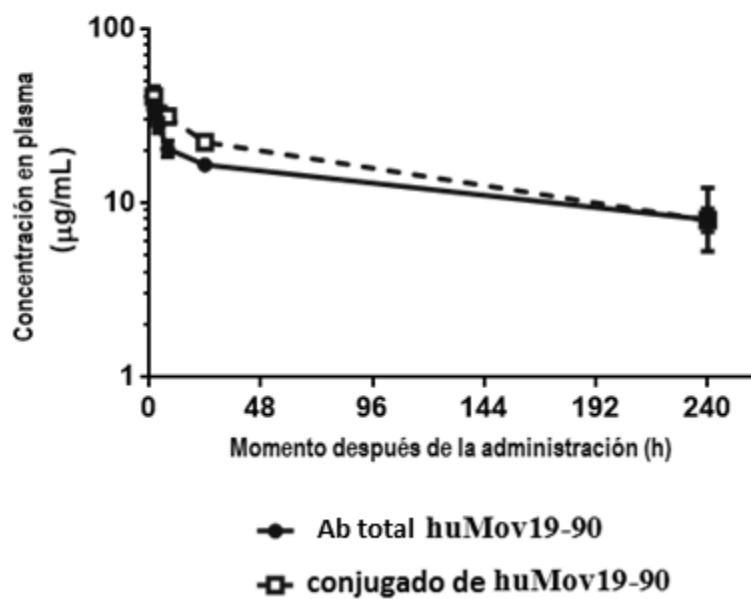


FIG. 19A

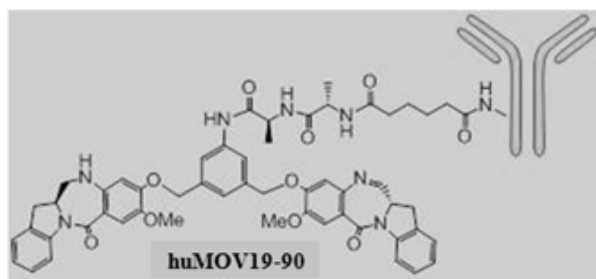


FIG. 19B

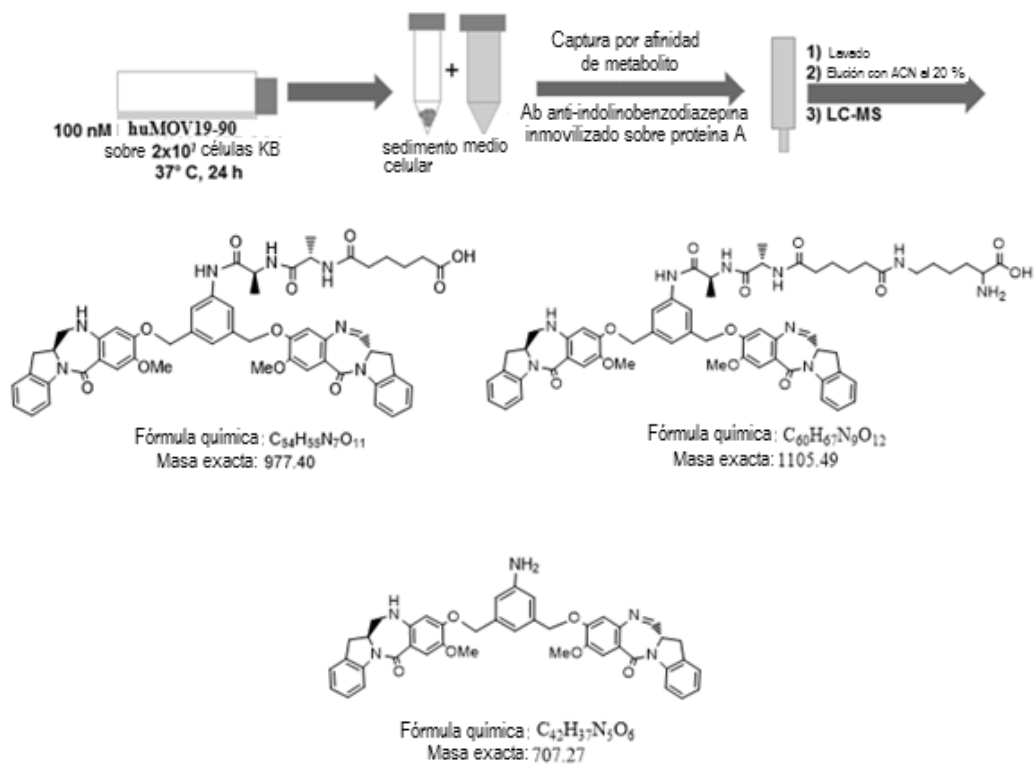


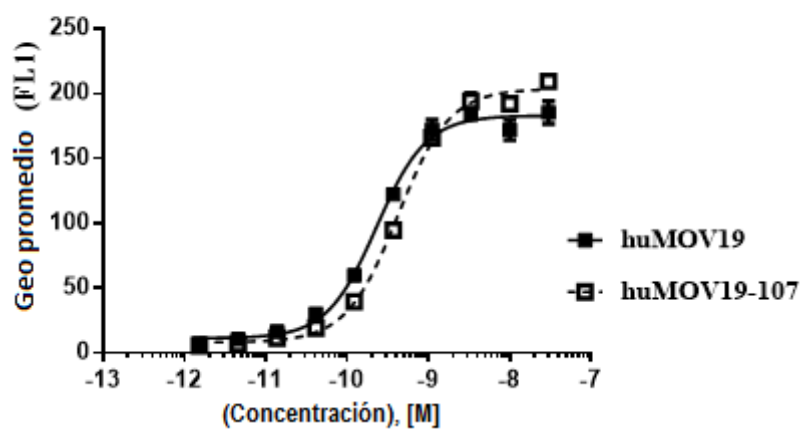
FIG. 20

FIG. 21

FIG. 21A Células Ishikawa

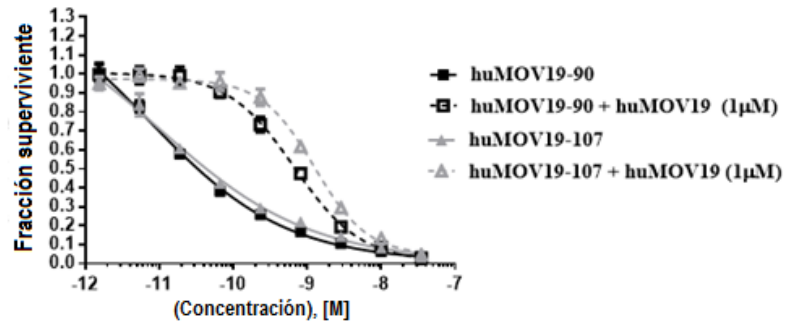


FIG. 21B Células KB

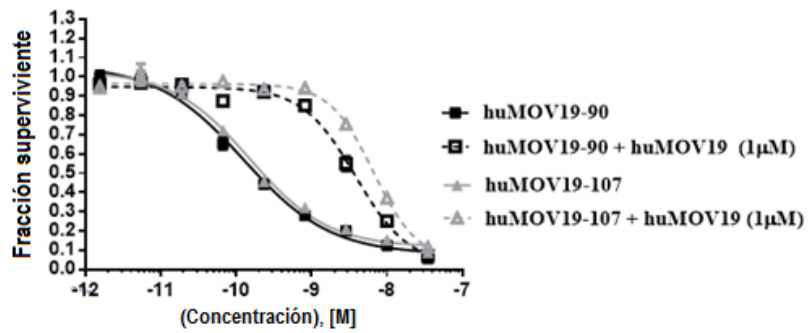
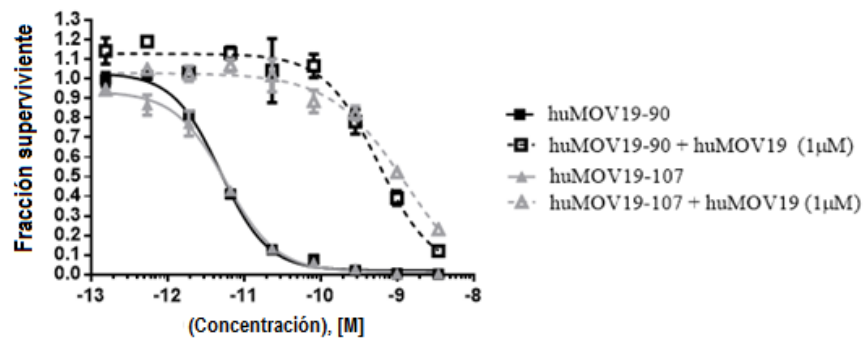
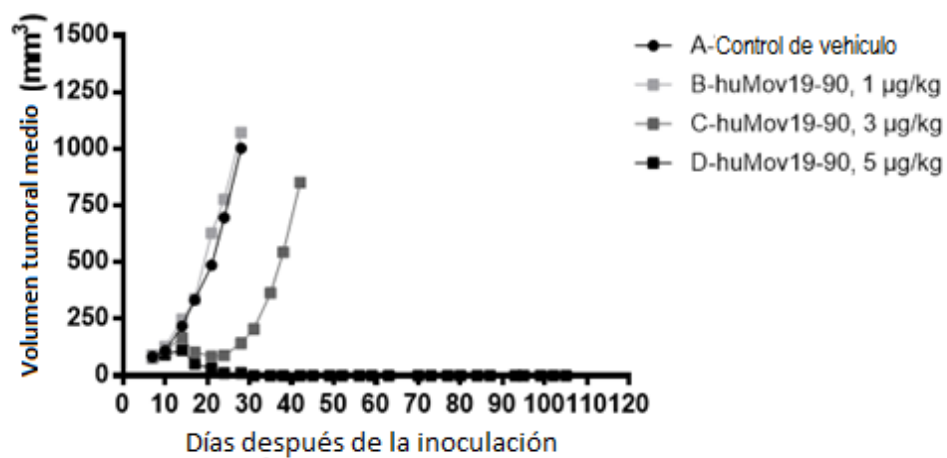
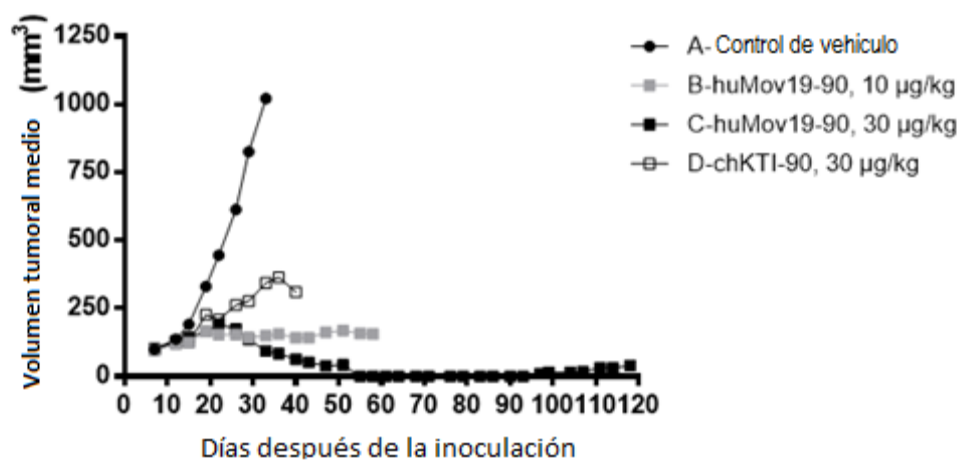


FIG. 22

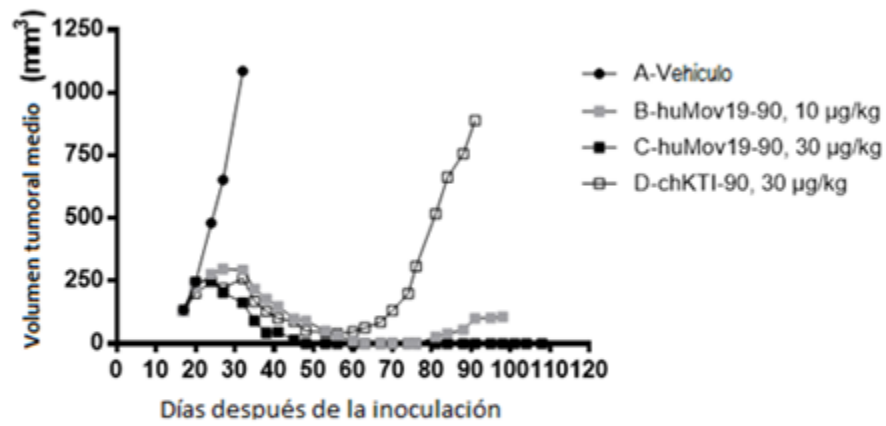


Grupo de tratamiento		Dosis (µg/kg)	T/C (Día 24)	Regresiones		Resultado
				PR	CR	
A	Control de vehiculo	—	—	—	—	—
B	huMov19-90	1	117%	0/6	0/6	Inactivo
C	huMov19-90	3	13%	1/6	0/6	Activo
D	huMov19-90	5	2%	6/6	4/6	Altamente activo

FIG. 23

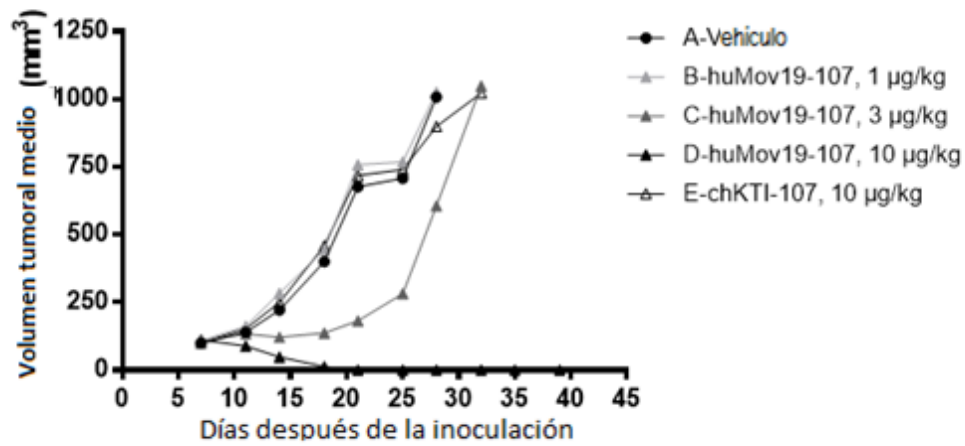
Grupo de tratamiento		Dosis (µg/kg)	T/C (Día 33)	Regresiones		Resultado
				PR	CR	
A	Control de vehículo I	-	-	-	-	-
B	huMov19-90	10	15%	1/6	0/6	Activo
C	huMov19-90	30	9%	6/6	6/6	Altamente activo
D	chKTI-90	30	34%	0/6	0/6	Activo

FIG. 24



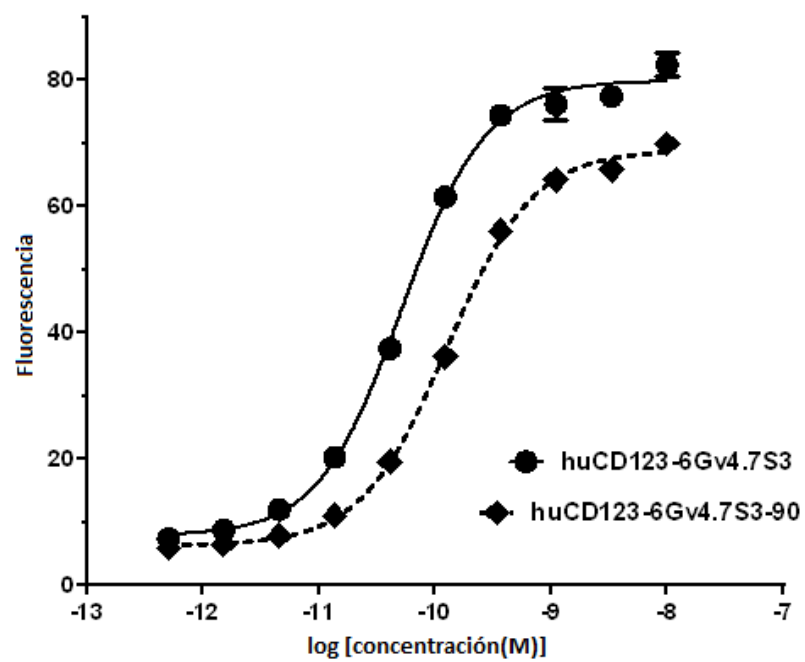
Treatment Group		Dosis (µg/kg)	T/C (Día 32)	Regresiones		Resultado
				PR	CR	
A	Control de vehiculo	-	-	-	-	-
E	huMov19-90	10	27%	6/6	6/6	Activo
F	huMov19-90	30	15%	6/6	6/6	Activo
G	chKTI-90	30	24%	4/6	0/6	Activo

FIG. 25



Grupo de tratamiento		Dosis (µg/kg)	T/C (Día 28)	Regresiones		Resultado
				PR	CR	
A	Control de vehículo	-	-	-	-	-
B	huMov19-107	1	102%	0/6	0/6	Inactivo
C	huMov19-107	3	60%	1/6	1/6	Inactivo
D	huMov19-107	10	0%	6/6	6/6	Altamente activo
E	chKTI-107	10	89%	0/6	0/6	Inactivo

FIG. 26



LISTADO DE SECUENCIAS

<110> ImmunoGen, Inc.

<120> DERIVADOS DE BENZODIAZEPINA CITOTÓXICOS

<130> 121162-02123

<150> 62/045,248

<151> 2014-09-03

<150> 62/087,040

<151> 2014-12-03

<150> 62/149,370

<151> 2014-04-17

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<151> 2014-05-20

<160> 29

<170> PatentIn versión 3.5

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<211> 5

<212> PRT

<213> Artificial

<220>

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se une específicamente a la cadena pesada CDR1 del receptor 1 de folato humano

<400> 1

Gly Tyr Phe Met Asn

1 5

<210> 2

<211> 17

<212> PRT

<213> Artificial

<220>

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<220>

<221> X

<222> (14)..(14)

<223> Lys, Gln, His, or Arg

<220>

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<222> (16)..(16)

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<220>

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<220>

<221> X

<222> (17)..(17)

<223> Gly, Glu, Thr, Ser, Ala, or Val

<400> 2

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1 5 10 15

Xaa

<210> 3

<211> 9

<212> PRT

<213> Artificial

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se une específicamente a la cadena pesada CDR3 del receptor 1 de folato humano

<400> 3

Tyr Asp Gly Ser Arg Ala Met Asp Tyr

1 5

<210> 4

<211> 15

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<220>

<223> anticuerpo humanizado o fragmento de unión al antígeno de este que
se une específicamente a la cadena ligera CDR1 del receptor 1 de folato humano

<400> 4

Lys Ala Ser Gln Ser Val Ser Phe Ala Gly Thr Ser Leu Met His

1 5 10 15

<210> 5

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se une específicamente a la cadena ligera CDR2 del receptor 1 de folato humano

<400> 5

Arg Ala Ser Asn Leu Glu Ala

1 5

<210> 6

<211> 9

<212> PRT

<213> Artificial

<220>

<223> anticuerpo humanizado o fragmento de unión al antígeno de este que

se une específicamente a la cadena ligera CDR3 del receptor 1 de folato humano

<400> 6

Gln Gln Ser Arg Glu Tyr Pro Tyr Thr

1 5

<210> 7

<211> 17

<212> PRT

<213> Artificial

<220>

<223> anticuerpo humanizado o fragmento de unión al antígeno de este preferido
que se une específicamente a la cadena pesada CDR2 del receptor 1 de folato humano

<400> 7

Arg Ile His Pro Tyr Asp Gly Asp Thr Phe Tyr Asn Gln Lys Phe Gln

1 5 10 15

Gly

<210> 8

<211> 448

<212> PRT

<213> Artificial

<220>

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un fragmento de unión al antígeno de este que se une específicamente a la
cadena pesada del receptor 1 de folato humano

<400> 8

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Val Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr

20 25 30

Phe Met Asn Trp Val Lys Gln Ser Pro Gly Gln Ser Leu Glu Trp Ile

35 40 45

Gly Arg Ile His Pro Tyr Asp Gly Asp Thr Phe Tyr Asn Gln Lys Phe

50 55 60

Gln Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Asn Thr Ala His

65 70 75 80

Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Phe Ala Val Tyr Tyr Cys

85 90 95

Thr Arg Tyr Asp Gly Ser Arg Ala Met Asp Tyr Trp Gly Gln Gly Thr

100 105 110

Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro

115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly

130

135

140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn

145

150

155

160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln

165

170

175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser

180

185

190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser

195

200

205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr

210

215

220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser

225

230

235

240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg

245 250 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro

260 265 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala

275 280 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val

290 295 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr

305 310 315 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr

325 330 335

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

340 345 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys

355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser

370

375

380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp

385

390

395

400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser

405

410

415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala

420

425

430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

435

440

445

<210> 9

<211> 218

<212> PRT

<213> Artificial

<220>

<223> anticuerpo del receptor anti-folato que es un anticuerpo humanizado o

un fragmento de unión al antígeno de este que se une específicamente a la
cadena ligera del receptor 1 de folato humano

<400> 9

Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Ala Val Ser Leu Gly

1 5 10 15

Gln Pro Ala Ile Ile Ser Cys Lys Ala Ser Gln Ser Val Ser Phe Ala

20 25 30

Gly Thr Ser Leu Met His Trp Tyr His Gln Lys Pro Gly Gln Gln Pro

35 40 45

Arg Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ala Gly Val Pro Asp

50 55 60

Arg Phe Ser Gly Ser Gly Ser Lys Thr Asp Phe Thr Leu Asn Ile Ser

65 70 75 80

Pro Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Arg

85 90 95

Glu Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg

100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln

115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr

130 135 140

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

145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr

165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys

180 185 190

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

195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

210 215

<210> 10

<211> 218

<212> PRT

<213> Artificial

<220>

<223> anticuerpo del receptor anti-folato que es un anticuerpo humanizado o
un fragmento de unión al antígeno de este que se une específicamente a la
cadena ligera del receptor 1 de folato humano

<400> 10

Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Ala Val Ser Leu Gly

1 5 10 15

Gln Pro Ala Ile Ile Ser Cys Lys Ala Ser Gln Ser Val Ser Phe Ala

20 25 30

Gly Thr Ser Leu Met His Trp Tyr His Gln Lys Pro Gly Gln Gln Pro

35 40 45

Arg Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ala Gly Val Pro Asp

50 55 60

Arg Phe Ser Gly Ser Gly Ser Lys Thr Asp Phe Thr Leu Thr Ile Ser

65 70 75 80

Pro Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Arg

85 90 95

Glu Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg

100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln

115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr

130 135 140

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

145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr

165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys

180 185 190

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

195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

210 215

<210> 11

<211> 118

<212> PRT

<213> Artificial

<220>

<223> anticuerpo del receptor anti-folato que es un anticuerpo humanizado o
un fragmento de unión al antígeno de este que se une específicamente al
dominio variable de cadena pesada del receptor 1 de folato humano

<400> 11

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Val Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr

20

25

30

Phe Met Asn Trp Val Lys Gln Ser Pro Gly Gln Ser Leu Glu Trp Ile

35

40

45

Gly Arg Ile His Pro Tyr Asp Gly Asp Thr Phe Tyr Asn Gln Lys Phe

50

55

60

Gln Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Asn Thr Ala His

65

70

75

80

Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Phe Ala Val Tyr Tyr Cys

85

90

95

Thr Arg Tyr Asp Gly Ser Arg Ala Met Asp Tyr Trp Gly Gln Gly Thr

100

105

110

Thr Val Thr Val Ser Ser

115

<210> 12

<211> 112

<212> PRT

<213> Artificial

<220>

<223> anticuerpo del receptor anti-folato que es un anticuerpo humanizado o un fragmento de unión al antígeno de este que se une específicamente al dominio variable de cadena ligera del receptor 1 de folato humano

<400> 12

Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Ala Val Ser Leu Gly

1 5 10 15

Gln Pro Ala Ile Ile Ser Cys Lys Ala Ser Gln Ser Val Ser Phe Ala

20 25 30

Gly Thr Ser Leu Met His Trp Tyr His Gln Lys Pro Gly Gln Gln Pro

35 40 45

Arg Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ala Gly Val Pro Asp

50 55 60

Arg Phe Ser Gly Ser Gly Ser Lys Thr Asp Phe Thr Leu Asn Ile Ser

65 70 75 80

Pro Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Arg

85

90

95

Glu Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg

100

105

110

<210> 13

<211> 112

<212> PRT

<213> Artificial

<220>

<223> anticuerpo del receptor anti-folato que es un anticuerpo humanizado o
un fragmento de unión al antígeno de este que se une específicamente al
dominio variable de cadena ligera del receptor 1 de folato humano

<400> 13

Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Ala Val Ser Leu Gly

1

5

10

15

Gln Pro Ala Ile Ile Ser Cys Lys Ala Ser Gln Ser Val Ser Phe Ala

20

25

30

Gly Thr Ser Leu Met His Trp Tyr His Gln Lys Pro Gly Gln Gln Pro

35 40 45

Arg Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ala Gly Val Pro Asp

50 55 60

Arg Phe Ser Gly Ser Gly Ser Lys Thr Asp Phe Thr Leu Thr Ile Ser

65 70 75 80

Pro Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Arg

85 90 95

Glu Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg

100 105 110

<210> 14

<211> 445

<212> PRT

<213> Artificial

<220>

<223> Anticuerpo: cadena pesada de longitud completa de huML66HC

<400> 14

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Leu Ser Leu Ala Ser Asn

20 25 30

Ser Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met

35 40 45

Gly Val Ile Trp Asn His Gly Gly Thr Asp Tyr Asn Pro Ser Ile Lys

50 55 60

Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu

65 70 75 80

Lys Met Asn Ser Leu Thr Ala Ala Asp Thr Ala Met Tyr Phe Cys Val

85 90 95

Arg Lys Gly Gly Ile Tyr Phe Asp Tyr Trp Gly Gln Gly Val Leu Val

100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala

115

120

125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu

130

135

140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly

145

150

155

160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser

165

170

175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu

180

185

190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr

195

200

205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr

210

215

220

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
225 230 235 240

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
 245 250 255

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
 260 265 270

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
 275 280 285

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
 290 295 300

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305 310 315 320

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
 325 330 335

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro

340 345 350

Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val

355 360 365

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly

370 375 380

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp

385 390 395 400

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp

405 410 415

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His

420 425 430

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

435 440 445

<210> 15

<211> 213

<212> PRT

<213> Artificial

<220>

<223> Anticuerpo: cadena ligera de longitud completa de huML66LC

<400> 15

Asp Thr Val Leu Thr Gln Ser Pro Ser Leu Ala Val Ser Pro Gly Glu

1 5 10 15

Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Ser Thr Leu Met

20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Gln Pro Lys Leu Leu Ile Tyr

35 40 45

Leu Ala Ser His Arg Glu Ser Gly Val Pro Ala Arg Phe Ser Gly Ser

50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Pro Met Glu Ala Glu

65 70 75 80

Asp Thr Ala Thr Tyr Tyr Cys Gln Gln Ser Arg Asn Asp Pro Trp Thr

85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Leu Lys Arg Thr Val Ala Ala Pro

100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr

115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys

130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu

145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser

165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala

180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe

195 200 205

Asn Arg Gly Glu Cys

210

<210> 16

<211> 448

<212> PRT

<213> Artificial

<220>

<223> cadena pesada de inmunoglobulina de anticuerpo anti-EGFR

<400> 16

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Ala Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr

20 25 30

Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Cys Ile

35 40 45

Gly Thr Ile Tyr Pro Gly Asp Gly Asp Thr Thr Tyr Thr Gln Lys Phe

50 55 60

Gln Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr

65 70 75 80

Met Gln Leu Ser Ser Leu Arg Ser Glu Asp Ser Ala Val Tyr Tyr Cys

85 90 95

Ala Arg Tyr Asp Ala Pro Gly Tyr Ala Met Asp Tyr Trp Gly Gln Gly

100 105 110

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe

115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu

130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp

145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu

165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser

180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro

195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys

210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro

225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser

245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp

260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn

275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val

290

295

300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu

305

310

315

320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys

325

330

335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr

340

345

350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr

355

360

365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu

370

375

380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu

385

390

395

400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys

405

410

415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu

420

425

430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

435

440

445

<210> 17

<211> 214

<212> PRT

<213> Artificial

<220>

<223> cadena ligera de inmunoglobulina de anticuerpo anti-EGFR

<400> 17

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 Gln Asp Ile Asn Asn Tyr

20

25

30

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

35

40

45

His Tyr Thr Ser Thr Leu His Pro Gly Ile Pro Ser Arg Phe Ser Gly

50

55

60

Ser Gly Ser Gly Arg Asp Tyr Ser Phe Ser Ile Ser Ser Leu Glu Pro

65

70

75

80

Glu Asp Ile Ala Thr Tyr Tyr Cys Leu Gln Tyr Asp Asn Leu Leu Tyr

85

90

95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala

100

105

110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly

115

120

125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala

130

135

140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln

145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser

165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr

180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser

195 200 205

Phe Asn Arg Gly Glu Cys

210

<210> 18

<211> 214

<212> PRT

<213> Artificial

<220>

<223> cadena ligera de inmunoglobulina de anticuerpo anti-EGFR

<400> 18

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 Gln Asp Ile Asn Asn Tyr

20 25 30

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

35 40 45

His Tyr Thr Ser Thr Leu His Pro Gly Ile Pro Ser Arg Phe Ser Gly

50 55 60

Ser Gly Ser Gly Arg Asp Tyr Ser Phe Ser Ile Ser Ser Leu Glu Pro

65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Leu Gln Tyr Asp Asn Leu Leu Tyr

85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala

100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly

115

120

125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala

130

135

140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln

145

150

155

160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser

165

170

175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr

180

185

190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser

195

200

205

Phe Asn Arg Gly Glu Cys

210

<210> 19

<211> 450

<212> PRT

<213> Artificial

<220>

<223> cadena pesada de anticuerpo anti-CD19

<400> 19

Gln Val Gln Leu Val Gln Pro Gly Ala Glu Val Val Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Leu Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Ser Asn

20 25 30

Trp Met His Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile

35 40 45

Gly Glu Ile Asp Pro Ser Asp Ser Tyr Thr Asn Tyr Asn Gln Asn Phe

50 55 60

Gln Gly Lys Ala Lys Leu Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr

65 70 75 80

Met Glu Val Ser Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys

85

90

95

Ala Arg Gly Ser Asn Pro Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln

100

105

110

Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val

115

120

125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala

130

135

140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser

145

150

155

160

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

165

170

175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro

180

185

190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys

195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp

210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly

225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile

245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu

260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His

275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg

290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys

305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu

325

330

335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr

340

345

350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu

355

360

365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp

370

375

380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val

385

390

395

400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp

405

410

415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His

420

425

430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro

435

440

445

Gly Lys

450

<210> 20

<211> 211

<212> PRT

<213> Artificial

<220>

<223> cadena ligera de anticuerpo anti-CD19

<400> 20

Glu Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly

1

5

10

15

Glu Arg Val Thr Met Thr Cys Ser Ala Ser Ser Gly Val Asn Tyr Met

20

25

30

His Trp Tyr Gln Gln Lys Pro Gly Thr Ser Pro Arg Arg Trp Ile Tyr

35

40

45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser

50

55

60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Ser Met Glu Pro Glu

65

70

75

80

Asp Ala Ala Thr Tyr Tyr Cys His Gln Arg Gly Ser Tyr Thr Phe Gly

85

90

95

Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val

100

105

110

Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser

115

120

125

Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln

130

135

140

Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val

145

150

155

160

Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu

165

170

175

Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu

180

185

190

Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg

195

200

205

Gly Glu Cys

210

<210> 21

<211> 447

<212> PRT

<213> Artificial

<220>

<223> cadena pesada de anticuerpo anti-Muc1

<400> 21

Gln Ala Gln Leu Val Gln Ser Gly Ala Glu Val Val Lys Pro Gly Ala

1

5

10

15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr

20 25 30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile

35 40 45

Gly Tyr Ile Tyr Pro Gly Asn Gly Ala Thr Asn Tyr Asn Gln Lys Phe

50 55 60

Gln Gly Lys Ala Thr Leu Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr

65 70 75 80

Met Gln Ile Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys

85 90 95

Ala Arg Gly Asp Ser Val Pro Phe Ala Tyr Trp Gly Gln Gly Thr Leu

100 105 110

Val Thr Val Ser Ala Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu

115 120 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys

130

135

140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser

145

150

155

160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser

165

170

175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser

180

185

190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn

195

200

205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His

210

215

220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val

225

230

235

240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr

245

250

255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu

260

265

270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys

275

280

285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser

290

295

300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys

305

310

315

320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile

325

330

335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro

340

345

350

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu

355 360 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn

370 375 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser

385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg

405 410 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu

420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

435 440 445

<210> 22

<211> 213

<212> PRT

<213> Artificial

<220>

<223> cadena ligera de anticuerpo anti-Muc1

<400> 22

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Met Ser Ala Ser Pro Gly

1 5 10 15

Glu Arg Val Thr Ile Thr Cys Ser Ala His Ser Ser Val Ser Phe Met

20 25 30

His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr

35 40 45

Ser Thr Ser Ser Leu Ala Ser Gly Val Pro Ala Arg Phe Gly Gly Ser

50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu

65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser Phe Pro Leu Thr

85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Thr Val Ala Ala Pro

100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr

115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys

130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu

145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser

165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala

180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe

195 200 205

Asn Arg Gly Glu Cys

210

<210> 23

<211> 447

<212> PRT

<213> Artificial

<220>

<223> cadena pesada de inmunoglobulina de anticuerpo anti-CD33

<400> 23

Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Val Val Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr

20 25 30

Tyr Ile His Trp Ile Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Val

35 40 45

Gly Val Ile Tyr Pro Gly Asn Asp Asp Ile Ser Tyr Asn Gln Lys Phe

50 55 60

Gln Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Thr Thr Ala Tyr

65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys

85 90 95

Ala Arg Glu Val Arg Leu Arg Tyr Phe Asp Val Trp Gly Gln Gly Thr

100 105 110

Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro

115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly

130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn

145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln

165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser

180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser

195

200

205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr

210

215

220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser

225

230

235

240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg

245

250

255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro

260

265

270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala

275

280

285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val

290

295

300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr

305 310 315 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr

325 330 335

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

340 345 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys

355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser

370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp

385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser

405 410 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala

420

425

430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

435

440

445

<210> 24

<211> 219

<212> PRT

<213> Artificial

<220>

<223> cadena ligera de inmunoglobulina de anticuerpo anti-CD33

<400> 24

Glu Ile Val Leu Thr Gln Ser Pro Gly Ser Leu Ala Val Ser Pro Gly

1

5

10

15

Glu Arg Val Thr Met Ser Cys Lys Ser Ser Gln Ser Val Phe Phe Ser

20

25

30

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

35

40

45

Ser Pro Arg Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val

50

55

60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr

65

70

75

80

Ile Ser Ser Val Gln Pro Glu Asp Leu Ala Ile Tyr Tyr Cys His Gln

85

90

95

Tyr Leu Ser Ser Arg Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

100

105

110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu

115

120

125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe

130

135

140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln

145

150

155

160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser

165

170

175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu

180

185

190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser

195

200

205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

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<211> 214

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<400> 25

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Val Gly

1

5

10

15

Glu Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Arg Ser Asn

20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Lys Leu Leu Val

35 40 45

Asn Val Ala Thr Asn Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly

50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Lys Ile Asn Ser Leu Gln Pro

65 70 75 80

Glu Asp Phe Gly Thr Tyr Tyr Cys Gln His Tyr Trp Gly Thr Thr Trp

85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala

100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly

115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala

130

135

140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln

145

150

155

160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser

165

170

175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr

180

185

190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser

195

200

205

Phe Asn Arg Gly Glu Cys

210

<210> 26

<211> 444

<212> PRT

<213> artificial

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<400> 26

Gln Val Gln Val Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln

1 5 10 15

Thr Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Thr Ser

20 25 30

Gly Val Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu

35 40 45

Gly Val Ile Trp Gly Asp Gly Ser Thr Asn Tyr His Pro Ser Leu Lys

50 55 60

Ser Arg Leu Ser Ile Lys Lys Asp His Ser Lys Ser Gln Val Phe Leu

65 70 75 80

Lys Leu Asn Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Tyr Cys Ala

85 90 95

Lys Gly Gly Tyr Ser Leu Ala His Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
115 120 125

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
130 135 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145 150 155 160

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
165 170 175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
180 185 190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
195 200 205

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys

210 215 220

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu

225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu

245 250 255

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys

260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys

275 280 285

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

290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys

305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys

325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser

340 345 350

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys

355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln

370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly

385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln

405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn

420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

435 440

<210> 27

<211> 444

<212> PRT

<213> artificial

<220>

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<400> 27

Gln Val Gln Val Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln

1 5 10 15

Thr Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Thr Ser

20 25 30

Gly Val Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu

35 40 45

Gly Val Ile Trp Gly Asp Gly Ser Thr Asn Tyr His Ser Ser Leu Lys

50 55 60

Ser Arg Leu Ser Ile Lys Lys Asp His Ser Lys Ser Gln Val Phe Leu

65 70 75 80

Lys Leu Asn Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Tyr Cys Ala

85

90

95

Lys Gly Gly Tyr Ser Leu Ala His Trp Gly Gln Gly Thr Leu Val Thr

100

105

110

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro

115

120

125

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val

130

135

140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala

145

150

155

160

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly

165

170

175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly

180

185

190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys

195

200

205

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys

210

215

220

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu

225

230

235

240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu

245

250

255

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys

260

265

270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys

275

280

285

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

290

295

300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys

305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys

325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser

340 345 350

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys

355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln

370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly

385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln

405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn

420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

435 440

<210> 28

<211> 213

<212> PRT

<213> artificial

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<400> 28

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Met Ser Ala Ser Pro Gly

1 5 10 15

Glu Arg Val Thr Met Thr Cys Ser Ala Thr Ser Ser Val Thr Tyr Met

20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Arg Trp Ile Tyr

35 40 45

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

50

55

60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu

65

70

75

80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Asp Asn Pro Pro Thr

85

90

95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro

100

105

110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr

115

120

125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys

130

135

140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu

145

150

155

160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser

165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala

180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe

195 200 205

Asn Arg Gly Glu Cys

210

<210> 29

<211> 449

<212> PRT

<213> artificial

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<400> 29

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Leu Lys Pro Ser Gln

1 5 10 15

Ser Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Gly

20

25

30

Phe Ala Trp His Trp Ile Arg Gln His Pro Gly Asn Lys Leu Glu Trp

35

40

45

Met Gly Tyr Ile Leu Tyr Ser Gly Ser Thr Val Tyr Ser Pro Ser Leu

50

55

60

Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn His Phe Phe

65

70

75

80

Leu Gln Leu Asn Ser Val Thr Ala Ala Asp Thr Ala Thr Tyr Tyr Cys

85

90

95

Ala Arg Gly Tyr Tyr Gly Tyr Gly Ala Trp Phe Ala Tyr Trp Gly Gln

100

105

110

Gly Thr Leu Val Thr Val Ser Ala Ala Ser Thr Lys Gly Pro Ser Val

115

120

125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala

130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser

145 150 155 160

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

165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro

180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys

195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp

210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly

225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile

245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu

260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His

275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg

290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys

305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu

325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr

340 345 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu

355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp

370

375

380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val

385

390

395

400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp

405

410

415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His

420

425

430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro

435

440

445

Gly