

1210303  
SEQUENCE LISTING

<110> F. Hoffmann-La Roche AG  
 <120> Self-controlled insulin delivery system  
 <130> case 24482  
 <160> 6  
 <170> PatentIn version 3.4  
 <210> 1  
 <211> 524  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> human GLUT2  
 <222> (1)..(524)

<400> 1

Met Thr Glu Asp Lys Val Thr Gly Thr Leu Val Phe Thr Val Ile Thr  
 1 5 10 15

Ala Val Leu Gly Ser Phe Gln Phe Gly Tyr Asp Ile Gly Val Ile Asn  
 20 25 30

Ala Pro Gln Gln Val Ile Ile Ser His Tyr Arg His Val Leu Gly Val  
 35 40 45

Pro Leu Asp Asp Arg Lys Ala Ile Asn Asn Tyr Val Ile Asn Ser Thr  
 50 55 60

Asp Glu Leu Pro Thr Ile Ser Tyr Ser Met Asn Pro Lys Pro Thr Pro  
 65 70 75 80

Trp Ala Glu Glu Glu Thr Val Ala Ala Ala Gln Leu Ile Thr Met Leu  
 85 90 95

Trp Ser Leu Ser Val Ser Ser Phe Ala Val Gly Gly Met Thr Ala Ser  
 100 105 110

Phe Phe Gly Gly Trp Leu Gly Asp Thr Leu Gly Arg Ile Lys Ala Met  
 115 120 125

Leu Val Ala Asn Ile Leu Ser Leu Val Gly Ala Leu Leu Met Gly Phe  
 130 135 140

Ser Lys Leu Gly Pro Ser His Ile Leu Ile Ile Ala Gly Arg Ser Ile  
 145 150 155 160

Ser Gly Leu Tyr Cys Gly Leu Ile Ser Gly Leu Val Pro Met Tyr Ile  
 165 170 175

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Gly Glu Ile Ala Pro Thr Ala Leu Arg Gly Ala Leu Gly Thr Phe His  
180 185 190

Gln Leu Ala Ile Val Thr Gly Ile Leu Ile Ser Gln Ile Ile Gly Leu  
195 200 205

Glu Phe Ile Leu Gly Asn Tyr Asp Leu Trp His Ile Leu Leu Gly Leu  
210 215 220

Ser Gly Val Arg Ala Ile Leu Gln Ser Leu Leu Leu Phe Phe Cys Pro  
225 230 235 240

Glu Ser Pro Arg Tyr Leu Tyr Ile Lys Leu Asp Glu Glu Val Lys Ala  
245 250 255

Lys Gln Ser Leu Lys Arg Leu Arg Gly Tyr Asp Asp Val Thr Lys Asp  
260 265 270

Ile Asn Glu Met Arg Lys Glu Arg Glu Glu Ala Ser Ser Glu Gln Lys  
275 280 285

Val Ser Ile Ile Gln Leu Phe Thr Asn Ser Ser Tyr Arg Gln Pro Ile  
290 295 300

Leu Val Ala Leu Met Leu His Val Ala Gln Gln Phe Ser Gly Ile Asn  
305 310 315 320

Gly Ile Phe Tyr Tyr Ser Thr Ser Ile Phe Gln Thr Ala Gly Ile Ser  
325 330 335

Lys Pro Val Tyr Ala Thr Ile Gly Val Gly Ala Val Asn Met Val Phe  
340 345 350

Thr Ala Val Ser Val Phe Leu Val Glu Lys Ala Gly Arg Arg Ser Leu  
355 360 365

Phe Leu Ile Gly Met Ser Gly Met Phe Val Cys Ala Ile Phe Met Ser  
370 375 380

Val Gly Leu Val Leu Leu Asn Lys Phe Ser Trp Met Ser Tyr Val Ser  
385 390 395 400

Met Ile Ala Ile Phe Leu Phe Val Ser Phe Phe Glu Ile Gly Pro Gly  
405 410 415

Pro Ile Pro Trp Phe Met Val Ala Glu Phe Phe Ser Gln Gly Pro Arg  
420 425 430

Pro Ala Ala Leu Ala Ile Ala Ala Phe Ser Asn Trp Thr Cys Asn Phe  
435 440 445

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Ile Val Ala Leu Cys Phe Gln Tyr Ile Ala Asp Phe Cys Gly Pro Tyr  
 450 455 460

Val Phe Phe Leu Phe Ala Gly Val Leu Leu Ala Phe Thr Leu Phe Thr  
 465 470 475 480

Phe Phe Lys Val Pro Glu Thr Lys Gly Lys Ser Phe Glu Glu Ile Ala  
 485 490 495

Ala Glu Phe Gln Lys Lys Ser Gly Ser Ala His Arg Pro Lys Ala Ala  
 500 505 510

Val Glu Met Lys Phe Leu Gly Ala Thr Glu Thr Val  
 515 520

<210> 2  
 <211> 496  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> human GLUT3  
 <222> (1)..(496)

<400> 2

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

Ala Thr Ile Gly Ser Phe Gln Phe Gly Tyr Asn Thr Gly Val Ile Asn  
 20 25 30

Ala Pro Glu Lys Ile Ile Lys Glu Phe Ile Asn Lys Thr Leu Thr Asp  
 35 40 45

Lys Gly Asn Ala Pro Pro Ser Glu Val Leu Leu Thr Ser Leu Trp Ser  
 50 55 60

Leu Ser Val Ala Ile Phe Ser Val Gly Gly Met Ile Gly Ser Phe Ser  
 65 70 75 80

Val Gly Leu Phe Val Asn Arg Phe Gly Arg Arg Asn Ser Met Leu Ile  
 85 90 95

Val Asn Leu Leu Ala Val Thr Gly Gly Cys Phe Met Gly Leu Cys Lys  
 100 105 110

Val Ala Lys Ser Val Glu Met Leu Ile Leu Gly Arg Leu Val Ile Gly  
 115 120 125

Leu Phe Cys Gly Leu Cys Thr Gly Phe Val Pro Met Tyr Ile Gly Glu  
 130 135 140

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Ile Ser Pro Thr Ala Leu Arg Gly Ala Phe Gly Thr Leu Asn Gln Leu  
145 150 155 160

Gly Ile Val Val Gly Ile Leu Val Ala Gln Ile Phe Gly Leu Glu Phe  
165 170 175

Ile Leu Gly Ser Glu Glu Leu Trp Pro Leu Leu Leu Gly Phe Thr Ile  
180 185 190

Leu Pro Ala Ile Leu Gln Ser Ala Ala Leu Pro Phe Cys Pro Glu Ser  
195 200 205

Pro Arg Phe Leu Leu Ile Asn Arg Lys Glu Glu Glu Asn Ala Lys Gln  
210 215 220

Ile Leu Gln Arg Leu Trp Gly Thr Gln Asp Val Ser Gln Asp Ile Gln  
225 230 235 240

Glu Met Lys Asp Glu Ser Ala Arg Met Ser Gln Glu Lys Gln Val Thr  
245 250 255

Val Leu Glu Leu Phe Arg Val Ser Ser Tyr Arg Gln Pro Ile Ile Ile  
260 265 270

Ser Ile Val Leu Gln Leu Ser Gln Gln Leu Ser Gly Ile Asn Ala Val  
275 280 285

Phe Tyr Tyr Ser Thr Gly Ile Phe Lys Asp Ala Gly Val Gln Glu Pro  
290 295 300

Ile Tyr Ala Thr Ile Gly Ala Gly Val Val Asn Thr Ile Phe Thr Val  
305 310 315 320

Val Ser Leu Phe Leu Val Glu Arg Ala Gly Arg Arg Thr Leu His Met  
325 330 335

Ile Gly Leu Gly Gly Met Ala Phe Cys Ser Thr Leu Met Thr Val Ser  
340 345 350

Leu Leu Leu Lys Asp Asn Tyr Asn Gly Met Ser Phe Val Cys Ile Gly  
355 360 365

Ala Ile Leu Val Phe Val Ala Phe Phe Glu Ile Gly Pro Gly Pro Ile  
370 375 380

Pro Trp Phe Ile Val Ala Glu Leu Phe Ser Gln Gly Pro Arg Pro Ala  
385 390 395 400

Ala Met Ala Val Ala Gly Cys Ser Asn Trp Thr Ser Asn Phe Leu Val  
405 410 415

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Gly Leu Leu Phe Pro Ser Ala Ala His Tyr Leu Gly Ala Tyr Val Phe  
                   420                  425                  430

Ile Ile Phe Thr Gly Phe Leu Ile Thr Phe Leu Ala Phe Thr Phe Phe  
           435                  440                  445

Lys Val Pro Glu Thr Arg Gly Arg Thr Phe Glu Asp Ile Thr Arg Ala  
       450                  455                  460

Phe Glu Gly Gln Ala His Gly Ala Asp Arg Ser Gly Lys Asp Gly Val  
       465                  470                  475                  480

Met Glu Met Asn Ser Ile Glu Pro Ala Lys Glu Thr Thr Thr Asn Val  
                   485                  490                  495

<210> 3  
 <211> 465  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> human glucokinase  
 <222> (1)..(465)

<400> 3

Met Leu Asp Asp Arg Ala Arg Met Glu Ala Ala Lys Lys Glu Lys Val  
 1                  5                  10                  15

Glu Gln Ile Leu Ala Glu Phe Gln Leu Gln Glu Glu Asp Leu Lys Lys  
           20                  25                  30

Val Met Arg Arg Met Gln Lys Glu Met Asp Arg Gly Leu Arg Leu Glu  
       35                  40                  45

Thr His Glu Glu Ala Ser Val Lys Met Leu Pro Thr Tyr Val Arg Ser  
       50                  55                  60

Thr Pro Glu Gly Ser Glu Val Gly Asp Phe Leu Ser Leu Asp Leu Gly  
       65                  70                  75                  80

Gly Thr Asn Phe Arg Val Met Leu Val Lys Val Gly Glu Gly Glu Glu  
           85                  90                  95

Gly Gln Trp Ser Val Lys Thr Lys His Gln Met Tyr Ser Ile Pro Glu  
           100                  105                  110

Asp Ala Met Thr Gly Thr Ala Glu Met Leu Phe Asp Tyr Ile Ser Glu  
       115                  120                  125

Cys Ile Ser Asp Phe Leu Asp Lys His Gln Met Lys His Lys Lys Leu  
       130                  135                  140

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Pro Leu Gly Phe Thr Phe Ser Phe Pro Val Arg His Glu Asp Ile Asp  
145 150 155 160

Lys Gly Ile Leu Leu Asn Trp Thr Lys Gly Phe Lys Ala Ser Gly Ala  
165 170 175

Glu Gly Asn Asn Val Val Gly Leu Leu Arg Asp Ala Ile Lys Arg Arg  
180 185 190

Gly Asp Phe Glu Met Asp Val Val Ala Met Val Asn Asp Thr Val Ala  
195 200 205

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

Ile Val Gly Thr Gly Cys Asn Ala Cys Tyr Met Glu Glu Met Gln Asn  
225 230 235 240

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

Trp Gly Ala Phe Gly Asp Ser Gly Glu Leu Asp Glu Phe Leu Leu Glu  
260 265 270

Tyr Asp Arg Leu Val Asp Glu Ser Ser Ala Asn Pro Gly Gln Gln Leu  
275 280 285

Tyr Glu Lys Leu Ile Gly Gly Lys Tyr Met Gly Glu Leu Val Arg Leu  
290 295 300

Val Leu Leu Arg Leu Val Asp Glu Asn Leu Leu Phe His Gly Glu Ala  
305 310 315 320

Ser Glu Gln Leu Arg Thr Arg Gly Ala Phe Glu Thr Arg Phe Val Ser  
325 330 335

Gln Val Glu Ser Asp Thr Gly Asp Arg Lys Gln Ile Tyr Asn Ile Leu  
340 345 350

Ser Thr Leu Gly Leu Arg Pro Ser Thr Thr Asp Cys Asp Ile Val Arg  
355 360 365

Arg Ala Cys Glu Ser Val Ser Thr Arg Ala Ala His Met Cys Ser Ala  
370 375 380

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

Val Met Arg Ile Thr Val Gly Val Asp Gly Ser Val Tyr Lys Leu His  
405 410 415

Pro Ser Phe Lys Glu Arg Phe His Ala Ser Val Arg Arg Leu Thr Pro  
420 425 430 1210303

Ser Cys Glu Ile Thr Phe Ile Glu Ser Glu Glu Gly Ser Gly Arg Gly  
435 440 445

Ala Ala Leu Val Ser Ala Val Ala Cys Lys Lys Ala Cys Met Leu Gly  
450 455 460

Gln  
465

<210> 4  
<211> 110  
<212> PRT  
<213> Homo sapiens

<220>  
<221> human insulin  
<222> (1)..(110)

<400> 4

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu  
1 5 10 15

Trp Gly Pro Asp Pro Ala Ala Ala Phe Val Asn Gln His Leu Cys Gly  
20 25 30

Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe  
35 40 45

Phe Tyr Thr Pro Lys Thr Arg Arg Glu Ala Glu Asp Leu Gln Val Gly  
50 55 60

Gln Val Glu Leu Gly Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu  
65 70 75 80

Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly Ile Val Glu Gln Cys Cys  
85 90 95

Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn  
100 105 110

<210> 5  
<211> 127  
<212> PRT  
<213> Homo sapiens

<220>  
<221> Pig preproinsulin  
<222> (1)..(127)

<400> 5

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Pro Ser Gly Thr Ser Cys Val Pro Arg Pro Pro Ala Ser Arg Ser Ser  
1 5 10 15

Pro Pro Ala Met Ala Leu Trp Thr Arg Leu Leu Pro Leu Leu Ala Leu  
20 25 30

Leu Ala Leu Trp Ala Pro Ala Pro Ala Gln Ala Phe Val Asn Gln His  
35 40 45

Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu  
50 55 60

Arg Gly Phe Phe Tyr Thr Pro Lys Ala Arg Arg Glu Ala Glu Asn Pro  
65 70 75 80

Gln Ala Gly Ala Val Glu Leu Gly Gly Gly Leu Gly Gly Leu Gln Ala  
85 90 95

Leu Ala Leu Glu Gly Pro Pro Gln Lys Arg Gly Ile Val Glu Gln Cys  
100 105 110

Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn  
115 120 125

<210> 6  
<211> 492  
<212> PRT  
<213> Homo sapiens

<220>  
<221> GLUT1  
<222> (1)..(492)

<400> 6

Met Glu Pro Ser Ser Lys Lys Leu Thr Gly Arg Leu Met Leu Ala Val  
1 5 10 15

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

Ile Asn Ala Pro Gln Lys Val Ile Glu Glu Phe Tyr Asn Gln Thr Trp  
35 40 45

Val His Arg Tyr Gly Glu Ser Ile Leu Pro Thr Thr Leu Thr Thr Leu  
50 55 60

Trp Ser Leu Ser Val Ala Ile Phe Ser Val Gly Gly Met Ile Gly Ser  
65 70 75 80

Phe Ser Val Gly Leu Phe Val Asn Arg Phe Gly Arg Arg Asn Ser Met  
85 90 95



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 Leu Met Met Asn Leu Leu Ala Phe Val Ser Ala Val Leu Met Gly Phe  
 100 105 110  
 Ser Lys Leu Gly Lys Ser Phe Glu Met Leu Ile Leu Gly Arg Phe Ile  
 115 120 125  
 Ile Gly Val Tyr Cys Gly Leu Thr Thr Gly Phe Val Pro Met Tyr Val  
 130 135 140  
 Gly Glu Val Ser Pro Thr Ala Phe Arg Gly Ala Leu Gly Thr Leu His  
 145 150 155 160  
 Gln Leu Gly Ile Val Val Gly Ile Leu Ile Ala Gln Val Phe Gly Leu  
 165 170 175  
 Asp Ser Ile Met Gly Asn Lys Asp Leu Trp Pro Leu Leu Leu Ser Ile  
 180 185 190  
 Ile Phe Ile Pro Ala Leu Leu Gln Cys Ile Val Leu Pro Phe Cys Pro  
 195 200 205  
 Glu Ser Pro Arg Phe Leu Leu Ile Asn Arg Asn Glu Glu Asn Arg Ala  
 210 215 220  
 Lys Ser Val Leu Lys Lys Leu Arg Gly Thr Ala Asp Val Thr His Asp  
 225 230 235 240  
 Leu Gln Glu Met Lys Glu Glu Ser Arg Gln Met Met Arg Glu Lys Lys  
 245 250 255  
 Val Thr Ile Leu Glu Leu Phe Arg Ser Pro Ala Tyr Arg Gln Pro Ile  
 260 265 270  
 Leu Ile Ala Val Val Leu Gln Leu Ser Gln Gln Leu Ser Gly Ile Asn  
 275 280 285  
 Ala Val Phe Tyr Tyr Ser Thr Ser Ile Phe Glu Lys Ala Gly Val Gln  
 290 295 300  
 Gln Pro Val Tyr Ala Thr Ile Gly Ser Gly Ile Val Asn Thr Ala Phe  
 305 310 315 320  
 Thr Val Val Ser Leu Phe Val Val Glu Arg Ala Gly Arg Arg Thr Leu  
 325 330 335  
 His Leu Ile Gly Leu Ala Gly Met Ala Gly Cys Ala Ile Leu Met Thr  
 340 345 350  
 Ile Ala Leu Ala Leu Leu Glu Gln Leu Pro Trp Met Ser Tyr Leu Ser  
 355 360 365

Ile Val Ala Ile Phe Gly Phe Val Ala Phe Phe Glu Val Gly Pro Gly  
 370 375 380

Pro Ile Pro Trp Phe Ile Val Ala Glu Leu Phe Ser Gln Gly Pro Arg  
 385 390 395 400

Pro Ala Ala Ile Ala Val Ala Gly Phe Ser Asn Trp Thr Ser Asn Phe  
 405 410 415

Ile Val Gly Met Cys Phe Gln Tyr Val Glu Gln Leu Cys Gly Pro Tyr  
 420 425 430

Val Phe Ile Ile Phe Thr Val Leu Leu Val Leu Phe Phe Ile Phe Thr  
 435 440 445

Tyr Phe Lys Val Pro Glu Thr Lys Gly Arg Thr Phe Asp Glu Ile Ala  
 450 455 460

Ser Gly Phe Arg Gln Gly Gly Ala Ser Gln Ser Asp Lys Thr Pro Glu  
 465 470 475 480

Glu Leu Phe His Pro Leu Gly Ala Asp Ser Gln Val  
 485 490