

# SEQUENCE LISTING

<110> Helsingin Yliopisto

<120> A cross-hybrid Fc-fusion polypeptide targeting PD-L1 and methods and uses related thereto

<130> BP302463

<160> 9

<170> PatentIn version 3.5

<210> 1

<211> 385

<212> PRT

<213> Artificial Sequence

<220>

<223> Fc-fusion polypeptide

<400> 1

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

Pro	Ala	Leu	Leu	Val	Val	Thr	Glu	Gly	Asp	Asn	Ala	Thr	Phe	Thr	Cys
		35					40					45			

Ser	Phe	Ser	Asn	Thr	Ser	Glu	Ser	Phe	His	Val	Val	Trp	His	Arg	Glu
	50					55					60				

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

Ser	Gln	Pro	Gly	Gln	Asp	Cys	Arg	Phe	Arg	Val	Thr	Gln	Leu	Pro	Asn
			85						90					95	

Gly	Arg	Asp	Phe	His	Met	Ser	Val	Val	Arg	Ala	Arg	Arg	Asn	Asp	Ser
			100					105					110		

Gly	Thr	Tyr	Val	Cys	Gly	Val	Ile	Ser	Leu	Ala	Pro	Lys	Ala	Gln	Ile
		115					120					125			

Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Gly Gly Gly  
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Pro Ala Pro Glu  
145 150 155 160

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Ala Leu Glu Asp  
165 170 175

Leu Leu Leu Gly Ser Glu Ala Asn Gly Val Thr Cys Val Val Val Asp  
180 185 190

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly  
195 200 205

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn  
210 215 220

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp  
225 230 235 240

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro  
245 250 255

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Ser Gly Asn Thr Phe  
260 265 270

Arg Pro Glu Val His Leu Leu Pro Pro Pro Ser Glu Glu Leu Ala Leu  
275 280 285

Asn Glu Leu Val Thr Leu Thr Cys Leu Ala Arg Gly Phe Ser Pro Lys  
290 295 300

Asp Val Leu Val Arg Trp Leu Gln Gly Ser Gln Glu Leu Pro Arg Glu  
305 310 315 320

Lys Tyr Leu Thr Trp Ala Ser Arg Gln Glu Pro Ser Gln Gly Thr Thr  
325 330 335

Thr Phe Ala Val Thr Ser Ile Leu Arg Val Ala Ala Glu Asp Trp Lys

340

345

350

Lys Gly Asp Thr Phe Ser Cys Met Val Gly His Glu Ala Leu Pro Leu  
 355 360 365

Ala Phe Thr Gln Lys Thr Ile Asp Arg His His His His His His  
 370 375 380

His  
 385

<210> 2  
 <211> 122  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> PD-1 ectodomain

<400> 2

Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr Phe Ser Pro Ala Leu  
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Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe Thr Cys Ser Phe Ser  
 20 25 30

Asn Thr Ser Glu Ser Phe His Val Val Trp His Arg Glu Ser Pro Ser  
 35 40 45

Gly Gln Thr Asp Thr Leu Ala Ala Phe Pro Glu Asp Arg Ser Gln Pro  
 50 55 60

Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu Pro Asn Gly Arg Asp  
 65 70 75 80

Phe His Met Ser Val Val Arg Ala Arg Arg Asn Asp Ser Gly Thr Tyr  
 85 90 95

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

Leu Arg Ala Glu Leu Arg Val Thr Glu Arg

115

120

<210> 3  
 <211> 221  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Fc of IgGA

<400> 3

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro  
 1 5 10 15

Ala Leu Glu Asp Leu Leu Leu Gly Ser Glu Ala Asn Gly Val Thr Cys  
 20 25 30

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp  
 35 40 45

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu  
 50 55 60

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu  
 65 70 75 80

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn  
 85 90 95

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Ser  
 100 105 110

Gly Asn Thr Phe Arg Pro Glu Val His Leu Leu Pro Pro Pro Ser Glu  
 115 120 125

Glu Leu Ala Leu Asn Glu Leu Val Thr Leu Thr Cys Leu Ala Arg Gly  
 130 135 140

Phe Ser Pro Lys Asp Val Leu Val Arg Trp Leu Gln Gly Ser Gln Glu  
 145 150 155 160

Leu Pro Arg Glu Lys Tyr Leu Thr Trp Ala Ser Arg Gln Glu Pro Ser

165

170

175

Gln Gly Thr Thr Thr Phe Ala Val Thr Ser Ile Leu Arg Val Ala Ala  
                   180                  185                  190

Glu Asp Trp Lys Lys Gly Asp Thr Phe Ser Cys Met Val Gly His Glu  
                   195                  200                  205

Ala Leu Pro Leu Ala Phe Thr Gln Lys Thr Ile Asp Arg  
           210                  215                  220

<210> 4

<211> 385

<212> PRT

<213> Artificial Sequence

<220>

<223> Modified (DF+TE) Fc-fusion polypeptide

<400> 4

Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Ala Leu Phe Arg Gly  
   1                  5                  10                  15

Val Gln Cys Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr Phe Ser  
                   20                  25                  30

Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe Thr Cys  
           35                  40                  45

Ser Phe Ser Asn Thr Ser Glu Ser Phe His Val Val Trp His Arg Glu  
           50                  55                  60

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

Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu Pro Asn  
                   85                  90                  95

Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn Asp Ser  
                   100                  105                  110

Gly Thr Tyr Val Cys Gly Val Ile Ser Leu Ala Pro Lys Ala Gln Ile

115

120

125

Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Gly Gly Gly  
 130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Pro Ala Pro Glu  
 145 150 155 160

Leu Leu Gly Gly Pro Asp Val Phe Leu Phe Pro Pro Ala Leu Glu Asp  
 165 170 175

Leu Leu Leu Gly Ser Glu Ala Asn Gly Val Thr Cys Val Val Val Asp  
 180 185 190

Val Ser Phe Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly  
 195 200 205

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn  
 210 215 220

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp  
 225 230 235 240

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Thr Asn Lys Ala Leu Pro  
 245 250 255

Ala Pro Glu Glu Lys Thr Ile Ser Lys Ala Lys Ser Gly Asn Thr Phe  
 260 265 270

Arg Pro Glu Val His Leu Leu Pro Pro Pro Ser Glu Glu Leu Ala Leu  
 275 280 285

Asn Glu Leu Val Thr Leu Thr Cys Leu Ala Arg Gly Phe Ser Pro Lys  
 290 295 300

Asp Val Leu Val Arg Trp Leu Gln Gly Ser Gln Glu Leu Pro Arg Glu  
 305 310 315 320

Lys Tyr Leu Thr Trp Ala Ser Arg Gln Glu Pro Ser Gln Gly Thr Thr  
 325 330 335

Thr Phe Ala Val Thr Ser Ile Leu Arg Val Ala Ala Glu Asp Trp Lys  
340 345 350

Lys Gly Asp Thr Phe Ser Cys Met Val Gly His Glu Ala Leu Pro Leu  
355 360 365

Ala Phe Thr Gln Lys Thr Ile Asp Arg His His His His His His  
370 375 380

His  
385

<210> 5  
<211> 221  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Modified (DF+TE) Fc of IgGA

<400> 5

Pro Ala Pro Glu Leu Leu Gly Gly Pro Asp Val Phe Leu Phe Pro Pro  
1 5 10 15

Ala Leu Glu Asp Leu Leu Leu Gly Ser Glu Ala Asn Gly Val Thr Cys  
20 25 30

Val Val Val Asp Val Ser Phe Glu Asp Pro Glu Val Lys Phe Asn Trp  
35 40 45

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu  
50 55 60

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu  
65 70 75 80

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Thr Asn  
85 90 95

Lys Ala Leu Pro Ala Pro Glu Glu Lys Thr Ile Ser Lys Ala Lys Ser  
100 105 110

Gly Asn Thr Phe Arg Pro Glu Val His Leu Leu Pro Pro Pro Ser Glu  
115 120 125

Glu Leu Ala Leu Asn Glu Leu Val Thr Leu Thr Cys Leu Ala Arg Gly  
130 135 140

Phe Ser Pro Lys Asp Val Leu Val Arg Trp Leu Gln Gly Ser Gln Glu  
145 150 155 160

Leu Pro Arg Glu Lys Tyr Leu Thr Trp Ala Ser Arg Gln Glu Pro Ser  
165 170 175

Gln Gly Thr Thr Thr Phe Ala Val Thr Ser Ile Leu Arg Val Ala Ala  
180 185 190

Glu Asp Trp Lys Lys Gly Asp Thr Phe Ser Cys Met Val Gly His Glu  
195 200 205

Ala Leu Pro Leu Ala Phe Thr Gln Lys Thr Ile Asp Arg  
210 215 220

<210> 6

<211> 663

<212> DNA

<213> Artificial Sequence

<220>

<223> Polynucleotide encoding the Fc region of the fusion polypeptide

<400> 6

cctgctccag aactgctcgg cggaccttcc gtgttcctgt ttccaccagc tctggaagat 60

ctgctgctgg gctctgaagc caatggcgtg acatgtgtgg tgggtggacgt gtcccacgag 120

gaccccgaag tgaagttcaa ttggtacgtg gacggcgtgg aagtgcacaa cgccaagacc 180

aagcctagag aggaacagta caacagcacc tacagagtgg tgtccgtgct gaccgtgctg 240

caccaggatt ggctgaacgg caaagagtac aagtgcaagg tgtccaacaa ggccctgcct 300

gctcctatcg agaaaacat cagcaaggcc aagagcggca acaccttcag acccgaagtg 360

catctgctgc ctccacctag cgaagaactg gccctgaatg agctgggtcac cctgacatgt 420

ctggccaggg gcttcagccc taaggatgtg ctcgttagat ggctgcaggg cagccaagag 480



ctgcccagag agaagtatct gacctgggcc agcagacaag agcctagcca gggcaccaca	540
acctttgccg tgaccagcat tctgagagtg gccgccgagg attggaagaa gggcgatacc	600
ttcagctgca tggtcggaca cgaagccctg cctctggcct tcacacagaa aacaatcgac	660
cgg	663

<210> 7  
 <211> 366  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Polynucleotide encoding the region of PD-1 of the fusion polypeptide

<400> 7	
gacagccctg acagaccttg gaaccctcca acattcagcc ccgctctgct ggtggttacc	60
gagggcgata atgccacctt cacctgtagc ttcagcaaca ccagcgagag cttccacgtc	120
gtgtggcaca gagagtctcc aagcggccag acagataccc tggctgcctt tcctgaggac	180
agatctcagc ccggccagga ctgcagattc agagtgaccc agctgcctaa cggccgggac	240
tttcacatga gcgtcgtgcg ggccagaaga aacgatagcg gcacatacgt gtgcggcgtg	300
atctctctgg cccctaaggc tcagatcaaa gagagcctga gagccgagct gagagtgacc	360
gaaaga	366

<210> 8  
 <211> 1158  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Polynucleotide encoding the Fc-fusion polypeptide

<400> 8	
atggaatttg gcctgagctg ggtgttcctg gtggccctgt ttagaggcgt gcagtgcgac	60
agccctgaca gaccttgga cctccaaca ttcagccccg ctctgctggt ggttaccgag	120
ggcgataatg ccaccttcac ctgtagcttc agcaacacca gcgagagctt ccacgtcgtg	180
tggcacagag agtctccaag cggccagaca gataccctgg ctgcctttcc tgaggacaga	240
tctcagcccc gccaggactg cagattcaga gtgaccacgc tgcctaacgg ccgggacttt	300
cacatgagcg tcgtgcgggc cagaagaaac gatagcggca catacgtgtg cggcgtgatc	360

tctctggccc ctaaggctca gatcaaagag agcctgagag ccgagctgag agtgaccgaa	420
agaggtggcg gaggatctgg cggaggtgga agcggcggag gcggatctga taagaccac	480
acctgtcctc catgtcctgc tccagaactg ctcggcggac cttccgtgtt cctgtttcca	540
ccagctctgg aagatctgct gctgggctct gaagccaatg gcgtgacatg tgtggtggtg	600
gacgtgtccc acgaggaccc cgaagtgaag ttcaattggt acgtggacgg cgtggaagtg	660
cacaacgcca agaccaagcc tagagaggaa cagtacaaca gcacctacag agtggtgtcc	720
gtgctgaccg tgctgcacca ggattggctg aacggcaaag agtacaagtg caaggtgtcc	780
aacaaggccc tgcctgctcc tatcgagaaa accatcagca aggccaagag cggcaacacc	840
ttcagacccg aagtgcattc gctgcctcca cctagcgaag aactggccct gaatgagctg	900
gtcacctga catgtctggc caggggcttc agccctaagg atgtgctcgt tagatggctg	960
cagggcagcc aagagctgcc cagagagaag tatctgacct gggccagcag acaagagcct	1020
agccagggca ccacaacctt tgccgtgacc agcattctga gagtggccgc cgaggattgg	1080
aagaagggcg ataccttcag ctgcatggtc ggacacgaag ccctgcctct ggccttcaca	1140
cagaaaacaa tcgaccgg	1158

<210> 9

<211> 1158

<212> DNA

<213> Artificial Sequence

<220>

<223> Polynucleotide encoding the modified (DF+TE) Fc-fusion  
polypeptide

<400> 9

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agccctgaca gaccttgga ccctccaaca ttacgccccg ctctgctggt ggttaccgag	120
ggcgataatg ccaccttcac ctgtagcttc agcaacacca gcgagagctt ccacgtcgtg	180
tggcacagag agtctccaag cggccagaca gataccctgg ctgcctttcc tgaggacaga	240
tctcagcccc gccaggactg cagattcaga gtgaccagc tgccaacgg ccgggacttt	300
cacatgagcg tcgtgcgggc cagaagaaac gatagcggca catacgtgtg cggcgtgatc	360
tctctggccc ctaaggctca gatcaaagag agcctgagag ccgagctgag agtgaccgaa	420

agaggtggcg gaggatctgg cggaggtgga agcggcggag gcggatctga taagaccac	480
acctgtcctc catgtcctgc tccagaactg ctcggcggac ccgatgtgtt cctgtttcca	540
ccagctctgg aagatctgct gctgggctct gaagccaatg gcgtgacatg tgtggtggtg	600
gacgtgtcct tcgaggaccc cgaagtgaag ttcaattggt acgtggacgg cgtggaagtg	660
cacaacgcca agaccaagcc tagagaggaa cagtacaaca gcacctacag agtggtgtcc	720
gtgctgaccg tgctgcacca ggattggctg aacggcaaag agtacaagtg caaagtgacc	780
aacaaggccc tgcctgctcc tgaggaaaag accatcagca aggccaagag cggcaacacc	840
ttcagacccg aagtgcattc gctgcctcca cctagcgaag aactggccct gaatgagctg	900
gtcaccctga catgtctggc caggggcttc agccctaagg atgtgctcgt tagatggctg	960
cagggcagcc aagagctgcc cagagagaag tatctgacct gggccagcag acaagagcct	1020
agccagggca ccacaacctt tgccgtgacc agcattctga gagtggccgc cgaggattgg	1080
aagaagggcg ataccttcag ctgcatggtc ggacacgaag ccctgcctct ggccttcaca	1140
cagaaaacca tcgaccgg	1158