

<110> LG CHEM, LTD.
 <120> FUSION POLYPEPTIDE COMPRISING Fc REGION OF IMMUNOGLOBULIN AND GDF15
 <130> OPP20200894KR
 <150> KR 10-2019-0047558
 <151> 2019-04-23
 <160> 18
 <170> KopatentIn 3.0
 <210> 1
 <211> 112
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> mature GDF15 (wild type)

<400> 1
 Ala Arg Asn Gly Asp His Cys Pro Leu Gly Pro Gly Arg Cys Cys Arg
 1 5 10 15
 Leu His Thr Val Arg Ala Ser Leu Glu Asp Leu Gly Trp Ala Asp Trp
 20 25 30
 Val Leu Ser Pro Arg Glu Val Gln Val Thr Met Cys Ile Gly Ala Cys
 35 40 45
 Pro Ser Gln Phe Arg Ala Ala Asn Met His Ala Gln Ile Lys Thr Ser
 50 55 60
 Leu His Arg Leu Lys Pro Asp Thr Val Pro Ala Pro Cys Cys Val Pro
 65 70 75 80
 Ala Ser Tyr Asn Pro Met Val Leu Ile Gln Lys Thr Asp Thr Gly Val
 85 90 95
 Ser Leu Gln Thr Tyr Asp Asp Leu Leu Ala Lys Asp Cys His Cys Ile
 100 105 110

<210> 2
 <211> 98

<212> PRT
<213> Artificial Sequence

<220>
<223> DeltaN14GDF15

<400> 2
Cys Arg Leu His Thr Val Arg Ala Ser Leu Glu Asp Leu Gly Trp Ala
1 5 10 15
Asp Trp Val Leu Ser Pro Arg Glu Val Gln Val Thr Met Cys Ile Gly
20 25 30
Ala Cys Pro Ser Gln Phe Arg Ala Ala Asn Met His Ala Gln Ile Lys
35 40 45
Thr Ser Leu His Arg Leu Lys Pro Asp Thr Val Pro Ala Pro Cys Cys
50 55 60
Val Pro Ala Ser Tyr Asn Pro Met Val Leu Ile Gln Lys Thr Asp Thr
65 70 75 80
Gly Val Ser Leu Gln Thr Tyr Asp Asp Leu Leu Ala Lys Asp Cys His
85 90 95
Cys Ile

<210> 3
<211> 217
<212> PRT
<213> Artificial Sequence

<220>
<223> human IgG1-Fc (UniProtKB P01857) CH2-CH3

<400> 3
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1 5 10 15
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
35 40 45
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu

50		55		60	
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His					
65		70		75	80
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys					
	85		90		95
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln					
	100		105		110
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu					
	115		120		125
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro					
	130		135		140
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn					
145		150		155	160
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu					
	165		170		175
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val					
	180		185		190
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln					
	195		200		205
Lys Ser Leu Ser Leu Ser Pro Gly Xaa					
	210		215		

<210> 4
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> human IgG1-Fc (UniProtKB P01857) Core Hinge

<400> 4
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro
 1 5 10

<210> 5
 <211> 217
 <212> PRT

<213> Artificial Sequence

<220>

<223> human IgG4-Fc (UniProtKB P01861) CH2-CH3 (general)

<220>

<221> MOD_RES

<222> (4)

<223> Xaa is Phe or Ala

<220>

<221> MOD_RES

<222> (5)

<223> Xaa is Leu or Ala

<220>

<221> MOD_RES

<222> (217)

<223> Xaa is absent or Lys

<400> 5

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

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30

Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr
35 40 45

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

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

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

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

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met
115 120 125

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

130	135	140
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn		
145	150	155 160
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		
	165	170 175
Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val		
	180	185 190
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
	195	200 205
Lys Ser Leu Ser Leu Ser Leu Gly Xaa		
210	215	

<210> 6
 <211> 217
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> human IgG4-Fc (UniProtKB P01861) CH2-CH3 (wild-type)

<400> 6
Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1 5 10 15
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30
Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr
35 40 45
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
50 55 60
Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65 70 75 80
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
85 90 95
Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
100 105 110
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met

115	120	125
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro		
130	135	140
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn		
145	150	155
Tyr Lys Thr Thr Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		
165	170	175
Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val		
180	185	190
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
195	200	205
Lys Ser Leu Ser Leu Ser Leu Gly Lys		
210	215	

<210> 7
 <211> 216
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> human IgG4-Fc (UniProtKB P01861) CH2-CH3 (mutated)

<400>	7
Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys	
1	15
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val	
20	30
Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr	
35	45
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu	
50	60
Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His	
65	80
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys	
85	95
Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln	

	100		105		110										
Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met
	115						120					125			
Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro
	130					135					140				
Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn
145					150					155					160
Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu
				165					170					175	
Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val
			180					185					190		
Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln
	195						200					205			
Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly								
	210					215									

<210> 8
 <211> 216
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> human IgG4-Fc (UniProtKB P01861) CH2-CH3 (mutated)

<400>	8														
Ala	Pro	Glu	Ala	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys
1				5					10					15	
Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val
			20					25					30		
Val	Val	Asp	Val	Ser	Gln	Glu	Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr
		35					40					45			
Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu
	50					55					60				
Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His
65					70					75					80
Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys

				85					90					95					
Gly	Leu	Pro	Ser	Ser	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln				
			100					105					110						
Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met				
		115					120					125							
Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro				
	130					135					140								
Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn				
145					150					155					160				
Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu				
				165					170						175				
Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val				
			180					185					190						
Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln				
		195					200					205							
Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly												
	210					215													

<210> 9
 <211> 216
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> human IgG4-Fc (UniProtKB P01861) CH2-CH3 (mutated)

<400>	9																		
Ala	Pro	Glu	Phe	Ala	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys				
1				5					10					15					
Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val				
			20					25					30						
Val	Val	Asp	Val	Ser	Gln	Glu	Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr				
		35					40					45							
Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu				
	50					55					60								
Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His				

65		70		75		80
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys						
	85		90		95	
Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln						
	100		105		110	
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met						
	115		120		125	
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro						
	130		135		140	
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn						
145		150		155		160
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu						
	165		170		175	
Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val						
	180		185		190	
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln						
	195		200		205	
Lys Ser Leu Ser Leu Ser Leu Gly						
	210		215			

<210> 10
 <211> 12
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> human IgG4-Fc (UniProtKB P01861) Hinge (general)

<220>
 <221> MOD_RES
 <222> (10)
 <223> Xaa is Ser or Pro

<400> 10
 Glu Ser Lys Tyr Gly Pro Pro Cys Pro Xaa Cys Pro
 1 5 10

<210> 11
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> human IgG4-Fc (UniProtKB P01861) Hinge (wild-type)

<400> 11
Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro
1 5 10

<210> 12
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> human IgG4-Fc (UniProtKB P01861) Hinge (mutated)

<400> 12
Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro
1 5 10

<210> 13
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> peptide linker

<400> 13
Gly Gly Gly Gly Ser
1 5

<210> 14
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> GDF15 coding gene

<400> 14
gcccggaaacg gcgaccactg cccctggggg cccggacggg gctgccggct gcacaccgtg 60
cgggcctccc tggaggacct gggctgggcc gactgggtgc tgtccccaag ggagggtgcaa 120
gtgaccatgt gcatcggcgc ctgcccattt cagttccggg ccgccaacat gcacgctcag 180
atcaagacca gcctgcaccg gctgaagccc gacaccgtgc ccgccccctg ctgcgtgccc 240
gcctcctaca accccatggg gctgattcag aagaccgaca ccggcgtgag cctgcagacc 300
tacgacgacc tgctggccaa ggactgccac tgcatctaa 339

<210> 15
<211> 678
<212> DNA
<213> Artificial Sequence

<220>
<223> IgG1-Fc coding gene

<400> 15
gacaaaaactc acacatgccc accgtgcccc gcacctgaac tcctgggggg accgtcagtc 60
ttcctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca 120
tgcgtggtgg tggacgtgag ccacgaagac cctgagggtca agttcaactg gtacgtggac 180
ggcgtggagg tgcataatgc caagacaaaag ccgcgggagg agcagtacaa cagcacgtac 240
cgtgtggtca gcgtcctcac cgtcctgcac caggactggc tgaatggcaa ggagtacaag 300
tgcaagggtct ccaacaaagc cctcccagcc cccatcgaga aaaccatctc caaagccaaa 360
gggcagcccc gagaaccaca ggtgtatacc ctgcccccat cccgggatga gctgaccaag 420
aaccagggtca gcctgacctg cctggtcaaa ggcttctatc ccagcgacat cgccgtggag 480
tgaggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt gctggactcc 540
gacggctcct tcttctctta cagcaagctc accgtggaca agagcagggtg gcagcagggg 600
aacgtcttct catgctccgt gatgcatgag gctctgcaca accactacac gcagaagagc 660
ctctccctgt ctccgggt 678

<210> 16
 <211> 684
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> IgG4-Fc coding gene

<400> 16
 gagtccaaat atggtccccc atgcccaccc tgcccagcac ctgaggccgc cgggggaccg 60
 tcagtcttcc tcttcccccc aaaacccaag gacaccctca tgatctcccg gacccttgag 120
 gtcacgtgcg tgggtggtgga cgtgtcccag gaggaccccg aggtgcagtt caactggtac 180
 gtggacggcg tggaggtgca caacgccaag accaagcccc gggaggagca gttcaactcc 240
 acctaccggg tgggtgtccgt gctgaccgtg ctgcaccagg actggctgaa cggcaaggag 300
 tacaagtgca aggtgtccaa caagggcctg ccctcctcca tcgagaagac catctccaag 360
 gccaagggcc agccccggga gccccaggtg tacaccctgc cccctccca ggaggagatg 420
 accaagaacc aggtgtccct gacctgcctg gtgaagggtt tctaccctc cgacatcgcc 480
 gtggagtggg agtccaacgg ccagcccgag aacaactaca agaccacccc ccccgctgctg 540
 gactccgacg gctccttctt cctgtactcc cggctgaccg tggacaagtc ccggtggcag 600
 gagggcaacg tgttctcctg ctccgtgatg cacgaggccc tgcacaacca ctacaccag 660
 aagtccctgt ccctgtccct gggc 684

<210> 17
 <211> 22
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Signal Peptide

<400> 17
 Met His Arg Pro Glu Ala Met Leu Leu Leu Leu Thr Leu Ala Leu Leu
 1 5 10 15
 Gly Gly Pro Thr Trp Ala
 20

<210> 18
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> peptide linker

<400> 18
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