

<110> AJOU UNIVERSITY INDUSTRY-ACADEMIC COOPERATION FOUNDATION
 <120> Heterodimeric Fc-fused cytokine and pharmaceutical composition comprising the same
 <130> PP-B1939
 <150> KR 2016-0101823
 <151> 2016-08-10
 <160> 20
 <170> KopatentIn 2.0
 <210> 1
 <211> 107
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> gamma4-EWRTV

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

<210> 2
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>

<223> gamma4-EWRVT

<400> 2

Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Ser Gln Glu
1 5 10 15

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
20 25 30

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
35 40 45

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe
50 55 60

Thr Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly
65 70 75 80

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
85 90 95

Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
100 105

<210> 3

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma4-EWRVTs-s

<400> 3

Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Gln Glu
1 5 10 15

Glu Met Thr Glu Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
20 25 30

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
35 40 45

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
50 55 60

Phe Leu Tyr Ser Trp Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly
65 70 75 80

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
85 90 95

Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
100 105

<210> 4
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> gamma4-EWRVTs-s

<400> 4
Gly Gln Pro Arg Glu Pro Arg Val Tyr Thr Leu Pro Pro Cys Gln Glu
1 5 10 15

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
20 25 30

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
35 40 45

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe
50 55 60

Thr Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly
65 70 75 80

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
85 90 95

Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
100 105

<210> 5
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> gamma4-A107

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

<210> 6
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> gamma4-A107

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

	85	90	95
Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys			
	100	105	
<210>	7		
<211>	107		
<212>	PRT		
<213>	Artificial Sequence		
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<223>	IgG1		
<400>	7		
Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp			
1	5	10	15
Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe			
	20	25	30
Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu			
	35	40	45
Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe			
	50	55	60
Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly			
65	70	75	80
Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr			
	85	90	95
Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys			
	100	105	

<210> 8
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> gamma1-A107

<400> 8
 Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
 1 5 10 15

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

<210> 9
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> gamma1-A107

<400> 9
 Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
 1 5 10 15
 Asn Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
 20 25 30
 Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
 35 40 45
 Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Val Ser Asp Gly Ser Phe
 50 55 60
 Thr Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
 65 70 75 80
 Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
 85 90 95
 Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 100 105

<210> 10
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> IgG2

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

<210> 11
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> gamma2-A107

<400> 11
 Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
 1 5 10 15
 Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Glu Gly Phe
 20 25 30

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
35 40 45

Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe
50 55 60

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

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
85 90 95

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
100 105

<210> 12
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> gamma2-A107

<400> 12
Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
1 5 10 15

Asn Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
20 25 30

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
35 40 45

Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Val Ser Asp Gly Ser Phe
50 55 60

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

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
85 90 95

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
100 105

<210> 13
<211> 107

<212> PRT
<213> Artificial Sequence

<220>
<223> IgG3

<400> 13
Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
1 5 10 15
Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
20 25 30
Tyr Pro Ser Asp Ile Ala Met Glu Trp Glu Ser Ser Gly Gln Pro Glu
35 40 45
Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
50 55 60
Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
65 70 75 80
Asn Ile Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
85 90 95
Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
100 105

<210> 14
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> gamma3-A107

<400> 14
Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
1 5 10 15
Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Glu Gly Phe
20 25 30
Tyr Pro Ser Asp Ile Ala Met Glu Trp Glu Ser Ser Gly Gln Pro Glu
35 40 45
Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe

50 55 60
 Phe Leu Tyr Ser Trp Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
 65 70 75 80
 Asn Ile Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
 85 90 95
 Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 100 105

<210> 15
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> gamma3-A107

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

<210> 16
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>

<223> IgG4

<400> 16

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu
1 5 10 15

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
20 25 30

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
35 40 45

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
50 55 60

Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly
65 70 75 80

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
85 90 95

Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
100 105

<210> 17

<211> 306

<212> PRT

<213> Artificial Sequence

<220>

<223> Mature human IL-12

<400> 17

Ile Trp Glu Leu Lys Lys Asp Val Tyr Val Val Glu Leu Asp Trp Tyr
1 5 10 15

Pro Asp Ala Pro Gly Glu Met Val Val Leu Thr Cys Asp Thr Pro Glu
20 25 30

Glu Asp Gly Ile Thr Trp Thr Leu Asp Gln Ser Ser Glu Val Leu Gly
35 40 45

Ser Gly Lys Thr Leu Thr Ile Gln Val Lys Glu Phe Gly Asp Ala Gly
50 55 60

Gln Tyr Thr Cys His Lys Gly Gly Glu Val Leu Ser His Ser Leu Leu
65 70 75 80

<213> Artificial Sequence

<220>

<223> Mature human IL-12

<400> 18

Arg Asn Leu Pro Val Ala Thr Pro Asp Pro Gly Met Phe Pro Cys Leu
1 5 10 15

His His Ser Gln Asn Leu Leu Arg Ala Val Ser Asn Met Leu Gln Lys
20 25 30

Ala Arg Gln Thr Leu Glu Phe Tyr Pro Cys Thr Ser Glu Glu Ile Asp
35 40 45

His Glu Asp Ile Thr Lys Asp Lys Thr Ser Thr Val Glu Ala Cys Leu
50 55 60

Pro Leu Glu Leu Thr Lys Asn Glu Ser Cys Leu Asn Ser Arg Glu Thr
65 70 75 80

Ser Phe Ile Thr Asn Gly Ser Cys Leu Ala Ser Arg Lys Thr Ser Phe
85 90 95

Met Met Ala Leu Cys Leu Ser Ser Ile Tyr Glu Asp Leu Lys Met Tyr
100 105 110

Gln Val Glu Phe Lys Thr Met Asn Ala Lys Leu Leu Met Asp Pro Lys
115 120 125

Arg Gln Ile Phe Leu Asp Gln Asn Met Leu Ala Val Ile Asp Glu Leu
130 135 140

Met Gln Ala Leu Asn Phe Asn Ser Glu Thr Val Pro Gln Lys Ser Ser
145 150 155 160

Leu Glu Glu Pro Asp Phe Tyr Lys Thr Lys Ile Lys Leu Cys Ile Leu
165 170 175

Leu His Ala Phe Arg Ile Arg Ala Val Thr Ile Asp Arg Val Met Ser
180 185 190

Tyr Leu Asn Ala Ser
195

<210> 19

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Mature mouse IL-12

<400> 19

Met Trp Glu Leu Glu Lys Asp Val Tyr Val Val Glu Val Asp Trp Thr
1 5 10 15

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

Glu Asp Asp Ile Thr Trp Thr Ser Asp Gln Arg His Gly Val Ile Gly
35 40 45

Ser Gly Lys Thr Leu Thr Ile Thr Val Lys Glu Phe Leu Asp Ala Gly
50 55 60

Gln Tyr Thr Cys His Lys Gly Gly Glu Thr Leu Ser His Ser His Leu
65 70 75 80

Leu Leu His Lys Lys Glu Asn Gly Ile Trp Ser Thr Glu Ile Leu Lys
85 90 95

Asn Phe Lys Asn Lys Thr Phe Leu Lys Cys Glu Ala Pro Asn Tyr Ser
100 105 110

Gly Arg Phe Thr Cys Ser Trp Leu Val Gln Arg Asn Met Asp Leu Lys
115 120 125

Phe Asn Ile Lys Ser Ser Ser Ser Ser Pro Asp Ser Arg Ala Val Thr
130 135 140

Cys Gly Met Ala Ser Leu Ser Ala Glu Lys Val Thr Leu Asp Gln Arg
145 150 155 160

Asp Tyr Glu Lys Tyr Ser Val Ser Cys Gln Glu Asp Val Thr Cys Pro
165 170 175

Thr Ala Glu Glu Thr Leu Pro Ile Glu Leu Ala Leu Glu Ala Arg Gln
180 185 190

Gln Asn Lys Tyr Glu Asn Tyr Ser Thr Ser Phe Phe Ile Arg Asp Ile
195 200 205

Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln Met Lys Pro Leu Lys Asn
210 215 220

Ser Gln Val Glu Val Ser Trp Glu Tyr Pro Asp Ser Trp Ser Thr Pro

	115		120		125										
Leu	Asp	Lys	Gly	Met	Leu	Val	Ala	Ile	Asp	Glu	Leu	Met	Gln	Ser	Leu
	130					135					140				
Asn	His	Asn	Gly	Glu	Thr	Leu	Arg	Gln	Lys	Pro	Pro	Val	Gly	Glu	Ala
145					150					155					160
Asp	Pro	Tyr	Arg	Val	Lys	Met	Lys	Leu	Cys	Ile	Leu	Leu	His	Ala	Phe
				165					170					175	
Ser	Thr	Arg	Val	Val	Thr	Ile	Asn	Arg	Val	Met	Gly	Tyr	Leu	Ser	Ser
			180					185					190		
Ala															