

6777020_1
SEQUENCE LISTING

<110> CHUGAI SEIYAKU KABUSHIKI KAISHA
<120> ANTIBODY VARIANT AND ISOFORM WITH LOWERED BIOLOGICAL ACTIVITY
<130> C1-A1719P
<150> JP 2017-212179
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Tyr Tyr Asp Ile Gln
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Ser Ile Ser Pro Ser Gly Gln Ser Thr Tyr Tyr Arg Arg Glu Val Lys
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Gly

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Arg Thr Gly Arg Glu Tyr Gly Gly Gly Trp Tyr Phe Asp Tyr
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Asp Asn Asn Met Asp
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Asp Ile Asn Thr Arg Ser Gly Gly Ser Ile Tyr Asn Glu Glu Phe Gln
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Asp

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Arg Lys Ser Tyr Gly Tyr Tyr Leu Asp Glu
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Lys Ala Ser Arg Asn Ile Glu Arg Gln Leu Ala
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Gln Ala Ser Arg Lys Glu Ser
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Gln Gln Tyr Ser Asp Pro Pro Leu Thr
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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Tyr Tyr
 20 25 30

Asp Ile Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

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

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Arg Thr Gly Arg Glu Tyr Gly Gly Gly Trp Tyr Phe Asp Tyr
 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
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185

190

Thr Val Pro₁₉₅ Ser Ser Ser Leu Gly₂₀₀ Thr Gln Thr Tyr Thr₂₀₅ Cys Asn Val
 Asp His₂₁₀ Lys Pro Ser Asn Thr₂₁₅ Lys Val Asp Lys Arg₂₂₀ Val Glu Ser Lys
 Tyr Gly₂₂₅ Pro Pro Cys Pro₂₃₀ Pro Cys Pro Ala Pro₂₃₅ Glu Phe Leu Gly₂₄₀ Gly
 Pro Ser Val Phe Leu₂₄₅ Phe Pro Pro Lys Pro₂₅₀ Lys Asp Thr Leu Met₂₅₅ Ile
 Ser Arg Thr Pro₂₆₀ Glu Val Thr Cys Val₂₆₅ Val Val Asp Val Ser₂₇₀ Gln Glu
 Asp Pro Glu₂₇₅ Val Gln Phe Asn Trp₂₈₀ Tyr Val Asp Gly Val₂₈₅ Glu Val His
 Asn Ala₂₉₀ Lys Thr Lys Pro Arg₂₉₅ Glu Glu Gln Tyr Asn₃₀₀ Ser Thr Tyr Arg
 Val₃₀₅ Val Ser Val Leu Thr₃₁₀ Val Leu His Gln Asp₃₁₅ Trp Leu Asn Gly Lys₃₂₀
 Glu Tyr Lys Cys Lys₃₂₅ Val Ser Asn Lys Gly₃₃₀ Leu Pro Ser Ser Ile₃₃₅ Glu
 Lys Thr Ile Ser₃₄₀ Lys Ala Lys Gly Gln₃₄₅ Pro Arg Glu Pro Gln₃₅₀ Val Tyr
 Thr Leu Pro₃₅₅ Pro Ser Gln Lys Glu Met Thr Lys Asn Gln₃₆₅ Val Ser Leu
 Thr Cys₃₇₀ Leu Val Lys Gly Phe₃₇₅ Tyr Pro Ser Asp Ile₃₈₀ Ala Val Glu Trp
 Glu₃₈₅ Ser Asn Gly Gln Pro₃₉₀ Glu Asn Asn Tyr Lys₃₉₅ Thr Thr Pro Pro Val₄₀₀
 Leu Asp Ser Asp Gly₄₀₅ Ser Phe Phe Leu Tyr₄₁₀ Ser Lys Leu Thr Val₄₁₅ Asp
 Lys Ser Arg Trp₄₂₀ Gln Glu Gly Asn Val₄₂₅ Phe Ser Cys Ser Val₄₃₀ Met His
 Glu Ala Leu₄₃₅ His Asn Arg Tyr Thr₄₄₀ Gln Lys Ser Leu Ser₄₄₅ Leu Ser Pro

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Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn
 20 25 30

Asn Met Asp Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Asp Ile Asn Thr Arg Ser Gly Gly Ser Ile Tyr Asn Glu Glu Phe
 50 55 60

Gln Asp Arg Val Ile Met Thr Val Asp Lys Ser Thr Asp Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr His Cys
 85 90 95

Ala Arg Arg Lys Ser Tyr Gly Tyr Tyr Leu Asp Glu Trp Gly Glu 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 Cys Ser Arg Ser Thr Ser Glu Ser 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 Thr Cys Asn Val Asp His Lys Pro
 195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro
 210 215 220

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

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Leu Phe Pro Pro Lys₂₄₅ Pro Lys Asp Thr Leu₂₅₀ Met Ile Ser Arg Thr₂₅₅ Pro

Glu Val Thr Cys₂₆₀ Val Val Val Asp Val₂₆₅ Ser Gln Glu Asp Pro₂₇₀ Glu Val

Gln Phe Asn₂₇₅ Trp Tyr Val Asp Gly₂₈₀ Val Glu Val His Asn₂₈₅ Ala Lys Thr

Lys Pro Arg Glu Glu Gln Tyr₂₉₅ Asn Ser Thr Tyr Arg₃₀₀ Val Val Ser Val

Leu Thr Val Leu His Gln₃₁₀ Asp Trp Leu Asn Gly₃₁₅ Lys Glu Tyr Lys Cys₃₂₀

Lys Val Ser Asn Lys₃₂₅ Gly Leu Pro Ser Ser₃₃₀ Ile Glu Lys Thr Ile₃₃₅ Ser

Lys Ala Lys Gly₃₄₀ Gln Pro Arg Glu Pro₃₄₅ Gln Val Tyr Thr Leu₃₅₀ Pro Pro

Ser Gln Glu₃₅₅ Glu Met Thr Lys Asn₃₆₀ Gln Val Ser Leu Thr₃₆₅ Cys Leu Val

Lys Gly₃₇₀ Phe Tyr Pro Ser Asp₃₇₅ Ile Ala Val Glu Trp₃₈₀ Glu Ser Asn Gly

Gln Pro Glu Asn Asn Tyr₃₉₀ Lys Thr Thr Pro Pro₃₉₅ Val Leu Asp Ser Asp₄₀₀

Gly Ser Phe Phe Leu₄₀₅ Tyr Ser Lys Leu Thr₄₁₀ Val Asp Lys Ser Arg₄₁₅ Trp

Gln Glu Gly Asn₄₂₀ Val Phe Ser Cys Ser₄₂₅ Val Met His Glu Ala₄₃₀ Leu His

Asn His Tyr₄₃₅ Thr Gln Glu Ser Leu₄₄₀ Ser Leu Ser Pro

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser₁₀ Leu Ser Ala Ser Val Gly₁₅
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Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Arg Asn Ile Glu Arg Gln
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20

25

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Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Glu Leu Leu Ile
 35 40 45

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

Ser Arg Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Asp Pro Pro Leu
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Val 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
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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Tyr Tyr
 20 25 30

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Asp Ile Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

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

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Arg Thr Gly Arg Glu Tyr Gly Gly Gly Trp Tyr Phe Asp Tyr
 100 105 110

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

Asn Met Asp Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Asp Ile Asn Thr Arg Ser Gly Gly Ser Ile Tyr Asn Glu Glu Phe
 50 55 60

Gln Asp Arg Val Ile Met Thr Val Asp Lys Ser Thr Asp Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr His Cys
 85 90 95

Ala Arg Arg Lys Ser Tyr Gly Tyr Tyr Leu Asp Glu Trp Gly Glu Gly
 100 105 110

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

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Glu Leu Leu Ile
35 40 45

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

Ser Arg Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Asp Pro Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105