

Supplemental information

Title:

Domain-level epitope mapping of polyclonal antibodies against HER-1 and HER-2 receptors using phage display technology

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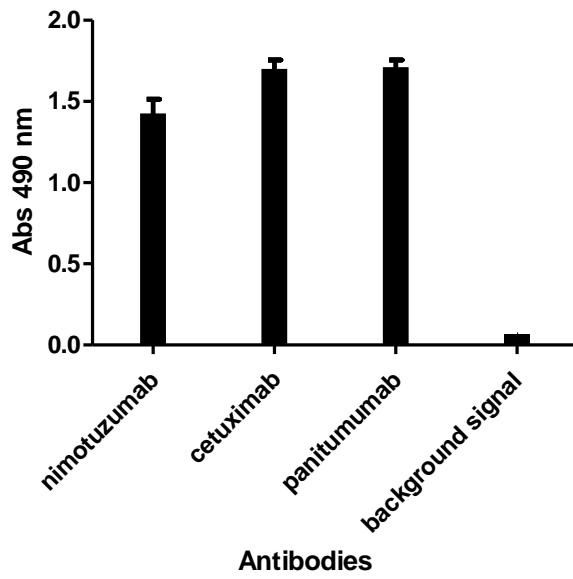
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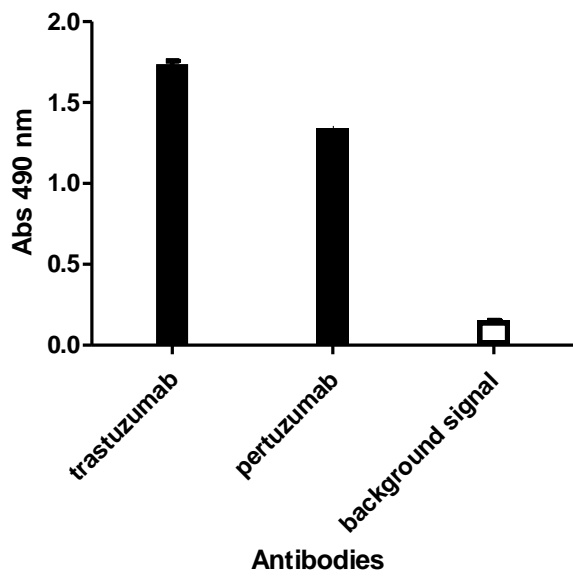
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a



b



Supplemental Figure 1. Reactivity of commercial antibodies against HER-1 and HER-2.

Polyvinyl chloride microtitration plates were coated with either HER-1 (a) or HER-2 (b) recombinant extracellular domains. Monoclonal antibodies (1 $\mu\text{g}/\text{mL}$) were incubated on coated plates and detected with an anti-human IgG antibody conjugated to horseradish peroxidase.

List of full DNA and deduced protein sequences of genetic constructs for phage display (from DsbA signal peptide to the end of M13 PVIII)

Color code:

DsbA signal peptide sequence

M13 PVIII sequence

Sequences of HER-1/HER-2 domains

c-myc tag sequence

NotI (GCGGCCGC) and SalI (GTCGAC) restriction sites

Changes introduced by site-directed mutagenesis on HER domains are underlined.

- Sequence 1: HER-1domain I

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCAGCTGAG
G A A A L E E K K V C Q G T S N K L T Q L
GGTGGGCGCCCTGGAGGAAAAGAAAGTTTGCCAAGGCACGAGTAACAAGCTCACGCAGTTG
G T F E D H F L S L Q R M F N N C E V V L
GGCACTTTTGAAGATCATTTTCTCAGCCTCCAGAGGATGTTCAATAACTGTGAGGTGGTCCTT
G N L E I T Y V Q R N Y D L S F L K T I Q
GGGAATTTGGAAATTACCTATGTGCAGAGGAATTATGATCTTTCCTTCTTAAAGACCATCCAG
E V A G Y V L I A L N T V E R I P L E N L
GAGGTGGCTGGTTATGTCCCTCATTGCCCTCAACACAGTGGAGCGAATTCCTTTGGAAAACCTG
Q I I R G N M Y Y E N S Y A L A V L S N Y
CAGATCATCAGAGGAAATATGTACTACGAAAATTCCTATGCCTTAGCAGTCTTATCTAACTAT
D A N K T G L K E L P M R N L Q E I L H G
GATGCAAATAAAACCGGACTGAAGGAGCTGCCCATGAGAAATTTACAGGAAATCCTGCATGGC
A V R F S N N P A L C N V E S I Q W R D I
GCCGTGCGGTTTCAGCAACAACCTGCCCTGTGCAACGTGGAGAGCATCCAGTGGCGGGACATA
V S S D F L S N M S M D F Q N H L G S C Q
GTCAGCAGTGACTTTCTCAGCAACATGTCGATGGACTTCCAGAACCACCTGGGCAGCTGCCAA
K C D P S C P N G S C W G A G E E N C Q K
AAGTGTGATCCAAGCTGTCCCAATGGGAGCTGCTGGGGTGCAGGAGAGGAGAACTGCCAGAAA
L T K I I V D D P G E Q K L I S E E D L N
CTGACCAAAATCATCGTCGACGATCCGGGGGAACAAAACTCATCTCAGAAGAGGATCTGAAT
G D P A K A A F D S L Q A S A T E Y I G Y
GGAATCCCGCAAAGCGGCCTTTGACTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTAT
A W A M V V V I V G A T I G I K L F K K F
CGGTGGGCGATGGTTGTTGTCATTGTGCGCGCAACTATCGGTATCAAGCTGTTTTAAGAAATTC
T S K A S
ACCTCGAAAGCAAGC

- Sequence 2: HER-1 domain II

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCACTGAG
G A A A C A Q Q C S G R C R G K S P S D C
GGTGGCGCCCTGTGCCAGCAGTGCTCCGGGCGCTGCCGTGGCAAGTCCCCAGTGACTGC
C H N Q C A A G C T G P R E S D C L V C R
TGCCACAACCAGTGTGCTGCAGGCTGCACAGGCCCCCGGGAGAGCGACTGCCTGGTCTGCCGC
K F R D E A T C K D T C P P L M L Y N P T
AAATTCGAGACGAAGCCACGTGCAAGGACACCTGCCCCCACTCATGCTCTACAACCCACC
T Y Q M D V N P E G K Y S F G A T C V K K
ACGTACCAGATGGATGTGAACCCCGAGGGCAAATACAGCTTTGGTGCCACCTGCGTGAAGAAG
C P R N Y V V T D H G S C V R A C G A D S
TGTCCCCGTAATTATGTGGTGACAGATCACGGCTCGTGCGTCCGAGCCTGTGGGGCCGACAGC
Y E M E E D G V R K C K K C E G P C R V D
TATGAGATGGAGGAAGACGGCGTCCGCAAGTGTAAGAAGTGCGAAGGGCCTTGCCGCCTCGAC
D P G E Q K L I S E E D L N G D P A K A A
GATCCGGGGGAACAAAACTCATCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAAGCGGCC
F D S L Q A S A T E Y I G Y A W A M V V V
TTTGA CTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGGCGATGGTTGTTGTC
I V G A T I G I K L F K K F T S K A S
ATTGTCGGCGCAACTATCGGTATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 3: HER-1domain III

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCACTGAG
G A A A K V C N G I G I G E F K D S L S I
GGTGGCGCCGCAAAGTGTGTAACGGAATAGGTATTGGTGAATTTAAAGACTCACTCTCCATA
N A T N I K H F K N C T S I S G D L H I L
AATGCTACGAATATTAACACTTCAAAAAGTGCACCTCCATCAGTGGCGATCTCCACATCCTG
P V A F R G D S F T H T P P L D P Q E L D
CCGGTGGCATTTAGGGGTGACTCCTTCACACATACTCCTCCTCTGGATCCACAGGAAGTGGAT
I L K T V K E I T G F L L I Q A W P E N R
ATTCTGAAAACCGTAAAGGAAATCACAGGGTTTTTGCTGATTCAGGCTTGGCCTGAAAACAGG
T D L H A F E N L E I I R G R T K Q H G Q
ACGGACCTCCATGCCTTTGAGAACCTAGAAATCATACGCGGCAGGACCAAGCAACATGGTCAG
F S L A V V S L N I T S L G L R S L K E I
TTTTCTCTTGCAGTCGTCAGCCTGAACATAACATCCTTGGGATTACGCTCCCTCAAGGAGATA
S D G D V I I S G N K N L C Y A N T I N W
AGTGATGGAGATGTGATAATTTAGGAAACAAAATTTGTGCTATGCAAATACAATAAACTGG
K K L F G T S G Q K T K I I S N R G E N S
AAAAAAGTTTGGGACCTCCGGTCAGAAAACAAAATTTATAAGCAACAGAGGTGAAAACAGC
C K A T G Q V C H A L C S P E G C W G P E
TGCAAGGCCACAGGCCAGGTCTGCCATGCCTTGTGCTCCCCGAGGGCTGCTGGGGCCCGGAG
P R D C V S C R N V S R G R E C V D K V D
CCCAGGGACTGCGTCTCTTGCCGGAATGTCAGCCAGGCAGGGAATGCGTGGACAAGGTCGAC
D P G E Q K L I S E E D L N G D P A K A A
GATCCGGGGGAACAAAAGTCACTCAGAAGAGGATCTGAATGGAGATCCCGCAAAGCGGCC
F D S L Q A S A T E Y I G Y A W A M V V V
TTTACTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGCGATGGTTGTTGTC
I V G A T I G I K L F K K F T S K A S
ATTGTCGGCGCAACTATCGGTATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 4: HER-1 domain IV

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCACTGAG
G A A A S C R N V S R G R E C V D K C N L
GGTGGCGCCGCTCTTGCCGGAATGTCAGCCGAGGCAGGGAATGCGTGGACAAGTGCAACCTT
L E G E P R E F V E N S E C I Q C H P E C
CTGGAGGGTGAGCCAAGGGAGTTTGTGGAGAACTCTGAGTGCATACAGTGCCACCCAGAGTGC
L P Q A M N I T C T G R G P D N C I Q C A
CTGCCTCAGGCCATGAACATCACCTGCACAGGACGGGGACCAGACAACCTGTATCCAGTGTGCC
H Y I D G P H C V K T C P A G V M G E N N
CACTACATTGACGGCCCCACTGCGTCAAGACCTGCCCCGGCAGGAGTCATGGGAGAAAACAAC
T L V W K Y A D A G H V C H L C H P N C T
ACCCTGGTCTGGAAGTACGCAGACGCCGGCCATGTGTGCCACCTGTGCCATCCAAACTGCACC
Y G C T G P G L E G C P T N G P K I P S V
TACGGATGCACTGGGCCAGGTCTTGAAGGCTGTCCAACGAATGGGCCTAAGATCCCGTCCGTC
D D P G E Q K L I S E E D L N G D P A K A
GACGATCCGGGGGAACAAAACTCATCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAAGCG
A F D S L Q A S A T E Y I G Y A W A M V V
GCCTTTGACTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGGCGATGGTTGTT
V I V G A T I G I K L F K K F T S K A S
GTCATTGTGGCGCAACTATCGGTATCAAGCTGTTTAAAGAAATTCACCTCGAAAGCAAGC

- Sequence 5: HER-2 domain I

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCA**GCTGAG**
G A A A T Q V C T G T D M K L R L P A S P
GGT**GCGGCCCGCC**ACCCAAGTGTGCACCGGCACAGACATGAAGCTGCGGCTCCCTGCCAGTCCC
E T H L D M L R H L Y Q G C Q V V Q G N L
GAGACCCACCTGGACATGCTCCGCCACCTCTACCAGGGCTGCCAGGTGGTGCAGGGAAACCTG
E L T Y L P T N A S L S F L Q D I Q E V Q
GAACTCACCTACCTGCCACCAATGCCAGCCTGTCTTCCCTGCAGGATATCCAGGAGGTGCAG
G Y V L I A H N Q V R Q V P L Q R L R I V
GGCTACGTGCTCATCGCTCACAACCAAGTGAGGCAGGTCCCACTGCAGAGGCTGCGGATTGTG
R G T Q L F E D N Y A L A V L D N G D P L
CGAGGCACCCAGCTCTTTGAGGACAACCTATGCCCTGGCCGTGCTAGACAATGGAGACCCGCTG
N N T T P V T G A S P G G L R E L Q L R S
AACAAATACCACCCCTGTCACAGGGGCTCCCCAGGAGGCCCTGCGGGAGCTGCAGCTTCGAAGC
L T E I L K G G V L I Q R N P Q L C Y Q D
CTCACAGAGATCTTGAAAGGAGGGGTCTTGATCCAGCGGAACCCCCAGCTCTGCTACCAGGAC
T I L W K D I F H K N N Q L A L T L I D T
ACGATTTTGTGGAAGGACATCTTCCACAAGAACAACCAGCTGGCTCTCACACTGATAGACACC
N R S R A C H P C S P M C K G S R C W G E
AACCGCTCTCGGGCCTGCCACCCCTGTTCTCCGATGTGTAAGGGCTCCCGCTGCTGGGGAGAG
S S E D C Q S L T R T V V D D P G E Q K L
AGTTCTGAGGATTGTCAGAGCCTGACGCGCACTGT**GTCGACGAT**CCGGGGGAACAAAAACTC
I S E E D L N G D P A K A A F D S L Q A S
ATCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAGCGGCCTTTGACTCCCTGCAAGCCTCA
A T E Y I G Y A W A M V V V I V G A T I G
GCGACCGAATATATCGGTTATGCGTGGGCGATGGTTGTTGTCATTGTCGGCGCAACTATCGGT
I K L F K K F T S K A S
ATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 6: HER-2 domain II

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCA**GCTGAG**
G A A A C A G G C A R C K G P L P T D C C
GGT**GCGGCCGC**CTGTGCCGGTGGCTGTGCCCGCTGCAAGGGGCCACTGCCCACTGACTGCTGC
H E Q C A A G C T G P K H S D C L A C L H
CATGAGCAGTGTGCTGCCGGCTGCACGGGGCCCAAGCACTCTGACTGCCTGGCCTGCCTCCAC
F N H S G I C E L H C P A L V T Y N T D T
TTCAACCACAGTGGCATCTGTGAGCTGCACTGCCAGCCCTGGTCACCTACAACACAGACACG
F E S M P N P E G R Y T F G A S C V T A C
TTTGAGTCCATGCCCAATCCCGAGGGCCGGTATACATTCGGCGCCAGCTGTGTGACTGCCTGT
P Y N Y L S T D V G S C T L V C P L H N Q
CCCTACAACCTACCTTTCTACGGACGTGGGATCCTGCACCCTCGTCTGCCCCCTGCACAACCAA
E V T A E D G T Q R C E K C S K P C A R V
GAGGTGACAGCAGAGGATGGAACACAGCGGTGTGAGAAGTGCAGCAAGCCCTGTGCCCGAGTC
D D P G E Q K L I S E E D L N G D P A K A
GACGATCCGGGG**GAACAAAACTCATCTCAGAAGAGGATCTGAATGGA**GATCCCGCAAAGCG
A F D S L Q A S A T E Y I G Y A W A M V V
GCCTTTGACTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGGCGATGGTTGTT
V I V G A T I G I K L F K K F T S K A S
GTCATTGTCCGGCGCAACTATCGGTATCAAGCTGTTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 7: HER-2 domain III

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCAGCTGAG
G A A A C Y G L G M E H L R E V R A V T S
GGTGCGGCCCGCTGCTATGGTCTGGGCATGGAGCACTTGGCAGAGGTGAGGGCAGTTACCAGT
A N I Q E F A G C K K I F G S L A F L P E
GCCAATATCCAGGAGTTTGCTGGCTGCAAGAAGATCTTTGGGAGCCTGGCATTCTGCCGGAG
S F D G D P A S N T A P L Q P E Q L Q V F
AGCTTTGATGGGGACCCAGCCTCCAACACTGCCCCGCTCCAGCCAGAGCAGCTCCAAGTGTTT
E T L E E I T G Y L Y I S A W P D S L P D
GAGACTCTGGAAGAGATCACAGGTTACCTATACATCTCAGCATGGCCGGACAGCCTGCCTGAC
L S V F Q N L Q V I R G R I L H N G A Y S
CTCAGCGTCTTCCAGAACCTGCAAGTAATCCGGGGACGAATTCTGCACAATGGCGCCTACTCG
L T L Q G L G I S W L G L R S L R E L G S
CTGACCCTGCAAGGGCTGGGCATCAGCTGGCTGGGGCTGCGCTCACTGAGGGAAGTGGGCAGT
G L A L I H H N T H L C F V H T V P W D Q
GGACTGGCCCTCATCCACCATAACACCCACCTCTGCTTCGTGCACACGGTGCCTGGGACCAG
L F R N P H Q A L L H T A N R P E D E C V
CTCTTTTCGGAACCCGCACCAAGCTCTGCTCCACACTGCCAACCGGCCAGAGGACGAGTGTGTG
G E G L A C H Q L C A R G H C W G P G P T
GGCGAGGGCCTGGCCTGCCACCAGCTGTGCGCCCGAGGGCACTGCTGGGGTCCAGGGCCCACC
Q C V N C S Q F L R G Q E C V E E V D D P
CAGTGTGTCAACTGCAGCCAGTTCCTTCGGGGCCAGGAGTGCCTGGAGGAAGTCGACGATCCG
G E Q K L I S E E D L N G D P A K A A F D
GGGGAACAAAACCTCATCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAGCGGCCTTTGAC
S L Q A S A T E Y I G Y A W A M V V V I V
TCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGGCGATGGTTGTTGTCATTGTC
G A T I G I K L F K K F T S K A S
GGCGCAACTATCGGTATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 8: HER-2 domain IV

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCAGCTGAG
G A A A C S Q F L R G Q E C V E E C R V L
GGTGGCGCCGCTGCAGCCAGTTCCTTCGGGGCCAGGAGTGCCTGGAGGAATGCCGAGTACTG
Q G L P R E Y V N A R H C L P C H P E C Q
CAGGGGCTCCCCAGGGAGTATGTGAATGCCAGGCACTGTTTGCCGTGCCACCCTGAGTGTGAG
P Q N G S V T C F G P E A D Q C V A C A H
CCCCAGAATGGCTCAGTGACCTGTTTTGGACCGGAGGCTGACCAGTGTGTGGCCTGTGCCAC
Y K D P P F C V A R C P S G V K P D L S Y
TATAAGGACCCCTCCCTTCTGCGTGGCCCGCTGCCCCAGCGGTGTGAAACCTGACCTCTCCTAC
M P I W K F P D E E G A C Q P C P I N C T
ATGCCCATCTGGAAGTTTCCAGATGAGGAGGGCGCATGCCAGCCTTGCCCCATCAACTGCACC
H S C V D L D D K G C P A E V D D P G E Q
CACTCCTGTGTGGACCTGGATGACAAGGGCTGCCCCGCCGAGGTCGACGATCCGGGGGAACAA
K L I S E E D L N G D P A K A A F D S L Q
AAACTCATCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAGCGGCCTTTGACTCCCTGCAA
A S A T E Y I G Y A W A M V V V I V G A T
GCCTCAGCGACCGAATATATCGGTTATGCGTGGGCGATGGTTGTTGTCATTGTGGCGCAACT
I G I K L F K K F T S K A S
ATCGGTATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 9: HER-1 domain III **S440L**

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCAGCTGAG
G A A A K V C N G I G I G E F K D S L S I
GGTGGCGCGCCAAAGTGTGTAACGGAATAGGTATTGGTGAATTTAAAGACTCACTCTCCATA
N A T N I K H F K N C T S I S G D L H I L
AATGCTACGAATATTAACACTTCAAAAACCTGCACCTCCATCAGTGGCGATCTCCACATCCTG
P V A F R G D S F T H T P P L D P Q E L D
CCGGTGGCATTTAGGGGTGACTCCTTACACATACTCCTCCTCTGGATCCACAGGAACCTGGAT
I L K T V K E I T G F L L I Q A W P E N R
ATTCTGAAAACCGTAAAGGAAATCACAGGGTTTTTGTCTGATTCAGGCTTGGCCTGAAAACAGG
T D L H A F E N L E I I R G R T K Q H G Q
ACGGACCTCCATGCCTTTGAGAACCTAGAAATCATACGCGGCAGGACCAAGCAACATGGTCAG
F S L A V V S L N I T S L G L R S L K E I
TTTTCTCTTGCAGTCGTCAGCCTGAACATAACATCCTTGGGATTACGCTCCCTCAAGGAGATA
S D G D V I I L G N K N L C Y A N T I N W
AGTGATGGAGATGTGATAATTCTGGGAAACAAAATTTGTGCTATGCAAATACAATAAACTGG
K K L F G T S G Q K T K I I S N R G E N S
AAAAAACTGTTTGGGACCTCCGGTCAGAAAACCAAATTTATAAGCAACAGAGGTGAAAACAGC
C K A T G Q V C H A L C S P E G C W G P E
TGCAAGGCCACAGGCCAGGTCTGCCATGCCTTGTGCTCCCCGAGGGCTGCTGGGGCCCGGAG
P R D C V S C R N V S R G R E C V D K V D
CCCAGGGACTGCGTCTCTTGCCGGAATGTCAGCCGAGGCAGGGAATGCGTGGACAAGGTCGAC
D P G E Q K L I S E E D L N G D P A K A A
GATCCGGGGGAACAAAAACTCATCTCAGAAGAGGATCTGAATGGA**GATCCCGCAAAAGCGGCC**
F D S L Q A S A T E Y I G Y A W A M V V V
TTTGACTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGGCGATGGTTGTTGTC
I V G A T I G I K L F K K F T S K A S
ATTGTCGGCGCAACTATCGGTATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 10: HER-1 domain III **G441R**

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCA**GCTGAG**
G A A A K V C N G I G I G E F K D S L S I
GGTGGCGCCG**CAAAGTGTGTAACGGAATAGGTATTGGTGAATTTAAAGACTCACTCTCCATA**
N A T N I K H F K N C T S I S G D L H I L
AATGCTACGAATATTAACACTTCAAAAAGTGCACCTCCATCAGTGGCGATCTCCACATCCTG
P V A F R G D S F T H T P P L D P Q E L D
CCGGTGGCATTTAGGGGTGACTCCTTCACACATACTCCTCCTCTGGATCCACAGGAAGTGGAT
I L K T V K E I T G F L L I Q A W P E N R
ATTCTGAAAACCGTAAAGGAAATCACAGGGTTTTTGCTGATTCAGGCTTGGCCTGAAAACAGG
T D L H A F E N L E I I R G R T K Q H G Q
ACGGACCTCCATGCCTTTGAGAACCTAGAAATCATACGCGGCAGGACCAAGCAACATGGTCAG
F S L A V V S L N I T S L G L R S L K E I
TTTTCTCTTGCAAGTCGTCAGCCTGAACATAACATCCTTGGGATTACGCTCCCTCAAGGAGATA
S D G D V I I S R N K N L C Y A N T I N W
AGTGATGGAGATGTGATAATTTCACGTAACAAAATTTGTGCTATGCAAATACAATAAACTGG
K K L F G T S G Q K T K I I S N R G E N S
AAAAAAGTTTGGGACCTCCGGTCAGAAAACCAAATTTATAAGCAACAGAGGTGAAAACAGC
C K A T G Q V C H A L C S P E G C W G P E
TGCAAGGCCACAGGCCAGGTCTGCCATGCCTTGTGCTCCCCGAGGGCTGCTGGGGCCCGGAG
P R D C V S C R N V S R G R E C V D K V D
CCCAGGGACTGCGTCTCTTGCCGGAATGTCAGCCGAGGCAGGGAATGCGTGGACAAG**GTCGAC**
D P G E Q K L I S E E D L N G D P A K A A
GATCCGGGG**GAACAAAAGTCACTCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAGCGGCC**
F D S L Q A S A T E Y I G Y A W A M V V V
TTTACTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGCGGATGGTTGTTGTC
I V G A T I G I K L F K K F T S K A S
ATTGTCGGCGCAACTATCGGTATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 11: HER-1 domain III **K443A**

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCA**GCTGAG**
G A A A K V C N G I G I G E F K D S L S I
GGT**GCGGCC**AAAGTGTGTAACGGAATAGGTATTGGTGAATTTAAAGACTCACTCTCCATA
N A T N I K H F K N C T S I S G D L H I L
AATGCTACGAATATTAACACTTCAAAA**ACTGCACCTCCATCAGTGGCGATCTCCACATCCTG**
P V A F R G D S F T H T P P L D P Q E L D
CCGGTGGCATTTAGGGGTGACTCCTT**CACACATACTCCTCCTCTGGATCCACAGGA**ACTGGAT****
I L K T V K E I T G F L L I Q A W P E N R
ATTCTGAAAACCGTAAAGGAAATCACAGGGTTTTTGCTGATTCAGGCTTGGCCTGAAAACAGG
T D L H A F E N L E I I R G R T K Q H G Q
ACGGACCTCCATGCCTTTGAGAACCTAGAAATC**ATACGCGGCAGGACCAAGCAACATGGTCAG**
F S L A V V S L N I T S L G L R S L K E I
TTTTCTCTTG**CAGTCGTCAGCCTGAACATAACATCCTTGGGATTACGCTCCCTCAAGGAGATA**
S D G D V I I S G N A N L C Y A N T I N W
AGTGATGGAGATGTGATAATTT**CAGGAAACCGGAATTTGTGCTATGCAAATACAATA**AACTGG****
K K L F G T S G Q K T K I I S N R G E N S
AAAA**AACTGTTTGGGACCTCCGGTCAGAAAACCAAAT**TATAAGCAACAGAGGTGAAAACAGC
C K A T G Q V C H A L C S P E G C W G P E
TGCAAGGCCACAGGCCAGGTCTGCCATGCCTTGTGCTCCCCGAGGGCTGCTGGGGCCCGGAG
P R D C V S C R N V S R G R E C V D K V D
CCCAGGGACTGCGTCTCTTGCCGGAATGTCAGCCAGGCAGGGAATGCGTGGACAAG**GTCGAC**
D P G E Q K L I S E E D L N G D P A K A A
GATCCGGGG**GAACAAAAACTCATCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAGCGGCC**
F D S L Q A S A T E Y I G Y A W A M V V V
TTT**GA**CTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGCGGATGGTTGTTGTC
I V G A T I G I K L F K K F T S K A S
ATTGTCGGCGCAACTATCGGTATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 12: HER-1 domain III **K443T**

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCA**GCTGAG**
G A A A K V C N G I G I G E F K D S L S I
GGT**GCGGCC**AAAGTGTGTAACGGAATAGGTATTGGTGAATTTAAAGACTCACTCTCCATA
N A T N I K H F K N C T S I S G D L H I L
AATGCTACGAATATTAACACTTCAAAA**ACTGCACCTCCATCAGTGGCGATCTCCACATCCTG**
P V A F R G D S F T H T P P L D P Q E L D
CCGGTGGCATTTAGGGGTGACTCCTT**CACACATACTCCTCCTCTGGATCCACAGGA**ACTGGAT****
I L K T V K E I T G F L L I Q A W P E N R
ATTCTGAAAACCGTAAAGGAAATCACAGGGTTTTTGCTGATTCAGGCTTGGCCTGAAAACAGG
T D L H A F E N L E I I R G R T K Q H G Q
ACGGACCTCCATGCCTTTGAGAACCTAGAAATC**ATACGCGGCAGGACCAAGCAACATGGTCAG**
F S L A V V S L N I T S L G L R S L K E I
TTTTCTCTTG**CAGTCGTCAGCCTGAACATAACATCCTTGGGATTACGCTCCCTCAAGGAGATA**
S D G D V I I S G N T N L C Y A N T I N W
AGTGATGGAGATGTGATAATTT**CAGGAAACACCA**ATTTGTGCTATGCAAATACAATA**AACTGG**
K K L F G T S G Q K T K I I S N R G E N S
AAAA**AACTGTTTGGGACCTCCGGTCAGAAAACCAA**AATTATAAGCAACAGAGGTGAAAACAGC
C K A T G Q V C H A L C S P E G C W G P E
TGCAAGGCCACAGGCCAGGTCTGCCATGCCTTGTGCTCCCCGAGGGCTGCTGGGGCCCGGAG
P R D C V S C R N V S R G R E C V D K V D
CCCAGGGACTGCGTCTCTTGCCGGAATGTCAGCCAGGCAGGGAATGCGTGGACAAG**GTCGAC**
D P G E Q K L I S E E D L N G D P A K A A
GATCCGGGG**GAACAAAAACTCATCTCAGAAGAGGATCTGAATGGAGATCCCGCAA**AGCGGCC
F D S L Q A S A T E Y I G Y A W A M V V V
TTT**ACTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGCGGATGGTTGTTGTC**
I V G A T I G I K L F K K F T S K A S
ATTGTCGGCGCAACTATCGGTATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 13: HER-1 domain III **I467M**

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCAGCTGAG
G A A A K V C N G I G I G E F K D S L S I
GGTGGCGCGCCAAAGTGTGTAACGGAATAGGTATTGGTGAATTTAAAGACTCACTCTCCATA
N A T N I K H F K N C T S I S G D L H I L
AATGCTACGAATATTAACACTTCAAAAACCTGCACCTCCATCAGTGGCGATCTCCACATCCTG
P V A F R G D S F T H T P P L D P Q E L D
CCGGTGGCATTTAGGGGTGACTCCTTACACATACTCCTCCTCTGGATCCACAGGAACCTGGAT
I L K T V K E I T G F L L I Q A W P E N R
ATTCTGAAAACCGTAAAGGAAATCACAGGGTTTTTGGCTGATTCAGGCTTGGCCTGAAAACAGG
T D L H A F E N L E I I R G R T K Q H G Q
ACGGACCTCCATGCCTTTGAGAACCTAGAAATCATACGCGGCAGGACCAAGCAACATGGTCAG
F S L A V V S L N I T S L G L R S L K E I
TTTTCTCTTGCAGTCGTCAGCCTGAACATAACATCCTTGGGATTACGCTCCCTCAAGGAGATA
S D G D V I I S G N A N L C Y A N T I N W
AGTGATGGAGATGTGATAATTTAGGAAACGCGAATTTGTGCTATGCAAATACAATAAACTGG
K K L F G T S G Q K T K I M S N R G E N S
AAAAAACTGTTTGGGACCTCCGGTCAGAAAACCAAATTTATGAGCAACAGAGGTGAAAACAGC
C K A T G Q V C H A L C S P E G C W G P E
TGCAAGGCCACAGGCCAGGTCTGCCATGCCTTGTGCTCCCCGAGGGCTGCTGGGGCCCGGAG
P R D C V S C R N V S R G R E C V D K V D
CCCAGGGACTGCGTCTCTTGCCGGAATGTCAGCCGAGGCAGGGAATGCGTGGACAAGGTCGAC
D P G E Q K L I S E E D L N G D P A K A A
GATCCGGGGGAACAAAAACTCATCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAAGCGGCC
F D S L Q A S A T E Y I G Y A W A M V V V
TTTGACTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGGCGATGGTTGTTGTC
I V G A T I G I K L F K K F T S K A S
ATTGTCGGCGCAACTATCGGTATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 14: HER-1 domain III **S468R**

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCA**GCTGAG**
G A A A K V C N G I G I G E F K D S L S I
GGT**GCGGCC**CAAAGTGTGTAACGGAATAGGTATTGGTGAATTTAAAGACTCACTCTCCATA
N A T N I K H F K N C T S I S G D L H I L
AATGCTACGAATATTAACACTTCAAAA**ACTGCACCTCCATCAGTGGCGATCTCCACATCCTG**
P V A F R G D S F T H T P P L D P Q E L D
CCGGTGGCATTTAGGGGTGACTCCTT**CACACATACTCCTCCTCTGGATCCACAGGA**ACTGGAT****
I L K T V K E I T G F L L I Q A W P E N R
ATTCTGAAAACCGTAAAGGAAATCACAGGGTTTTTGCTGATTCAGGCTTGGCCTGAAAACAGG
T D L H A F E N L E I I R G R T K Q H G Q
ACGGACCTCCATGCCTTTGAGAACCTAGAAATC**ATACGCGGCAGGACCAAGCAACATGGTCAG**
F S L A V V S L N I T S L G L R S L K E I
TTTTCTCTTGCAGTCGTCAGCCTGAACATAACATCCTTGGGATTACGCTCCCTCAAGGAGATA
S D G D V I I S G N A N L C Y A N T I N W
AGTGATGGAGATGTGATAATTT**CAGGAAACGCGAATTTGTGCTATGCAAATACAATAAACTGG**
K K L F G T S G Q K T K I I R N R G E N S
AAAA**ACTGTTTGGGACCTCCGGTCAGAAAACCAAAT**TATACGTAACAGAGGTGAAAACAGC
C K A T G Q V C H A L C S P E G C W G P E
TGCAAGGCCACAGGCCAGGTCTGCCATGCCTTGTGCTCCCCGAGGGCTGCTGGGGCCCGGAG
P R D C V S C R N V S R G R E C V D K V D
CCCAGGGACTGCGTCTCTT**GCCGGAATGTCAGCCAGGCAGGGAATGCGTGGACAAGGTCGAC**
D P G E Q K L I S E E D L N G D P A K A A
GATCCGGGG**GAACAAAAACTCATCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAGCGGCC**
F D S L Q A S A T E Y I G Y A W A M V V V
TTT**ACTCCCTGCAAGCCTCAGCGACCGAATATATCGGTTATGCGTGGCGATGGTTGTTGTC**
I V G A T I G I K L F K K F T S K A S
ATTGTCGGCGCAACTATCGGTATCAAGCTGTTTAAGAAATTCACCTCGAAAGCAAGC

- Sequence 15: HER-2 domain IV **D560A**

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCAGCTGAG
G A A A C S Q F L R G Q E C V E E C R V L
GGTGGCGCCGCTGCAGCCAGTTCCTTCGGGGCCAGGAGTGCCTGGAGGAATGCCGAGTACTG
Q G L P R E Y V N A R H C L P C H P E C Q
CAGGGGCTCCCCAGGGAGTATGTGAATGCCAGGCACTGTTTGCCGTGCCACCCTGAGTGTGAG
P Q N G S V T C F G P E A A Q C V A C A H
CCCCAGAATGGCTCAGTGACCTGTTTTGGACCGGAGGCTGCGCAGTGTGTGGCCTGTGCCAC
Y K D P P F C V A R C P S G V K P D L S Y
TATAAGGACCCCTCCCTTCTGCGTGGCCCGCTGCCCCAGCGGTGTGAAACCTGACCTCTCCTAC
M P I W K F P D E E G A C Q P C P I N C T
ATGCCCATCTGGAAGTTTCCAGATGAGGAGGGCGCATGCCAGCCTTGCCCCATCAACTGCACC
H S C V D L D D K G C P A E V D D P G E Q
CACTCCTGTGTGGACCTGGATGACAAGGGCTGCCCCGCCGAGGTCGACGATCCGGGGGAACAA
K L I S E E D L N G D P A K A A F D S L Q
AAACTCATCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAGCGGCCTTTGACTCCCTGCAA
A S A T E Y I G Y A W A M V V V I V G A T
GCCTCAGCGACCGAATATATCGGTTATGCGTGGGCGATGGTTGTTGTCATTGTGGCGCAACT
I G I K L F K K F T S K A S
ATCGGTATCAAGCTGTTTAAAGAAATTCACCTCGAAAGCAAGC

- Sequence 16: HER-2 domain IV **D560N**

M K K I W L A L A G L V L A F S A S A A E
ATGAAAAAGATTTGGCTGGCGCTGGCTGGTTTAGTTTTAGCGTTTAGCGCAAGTGCAGCTGAG
G A A A C S Q F L R G Q E C V E E C R V L
GGTGGCGCCGCTGCAGCCAGTTCCTTCGGGGCCAGGAGTGCCTGGAGGAATGCCGAGTACTG
Q G L P R E Y V N A R H C L P C H P E C Q
CAGGGGCTCCCCAGGGAGTATGTGAATGCCAGGCACTGTTTGCCGTGCCACCCTGAGTGTGAG
P Q N G S V T C F G P E A N Q C V A C A H
CCCCAGAATGGCTCAGTGACCTGTTTTGGACCGGAGGCTAACCAGTGTGTGGCCTGTGCCAC
Y K D P P F C V A R C P S G V K P D L S Y
TATAAGGACCCCTCCCTTCTGCGTGGCCCGCTGCCCCAGCGGTGTGAAACCTGACCTCTCCTAC
M P I W K F P D E E G A C Q P C P I N C T
ATGCCCATCTGGAAGTTTCCAGATGAGGAGGGCGCATGCCAGCCTTGCCCCATCAACTGCACC
H S C V D L D D K G C P A E V D D P G E Q
CACTCCTGTGTGGACCTGGATGACAAGGGCTGCCCCGCCGAGGTCGACGATCCGGGGGAACAA
K L I S E E D L N G D P A K A A F D S L Q
AAACTCATCTCAGAAGAGGATCTGAATGGAGATCCCGCAAAGCGGCCTTTGACTCCCTGCAA
A S A T E Y I G Y A W A M V V V I V G A T
GCCTCAGCGACCGAATATATCGGTTATGCGTGGGCGATGGTTGTTGTCATTGTGGCGCAACT
I G I K L F K K F T S K A S
ATCGGTATCAAGCTGTTTAAAGAAATTCACCTCGAAAGCAAGC