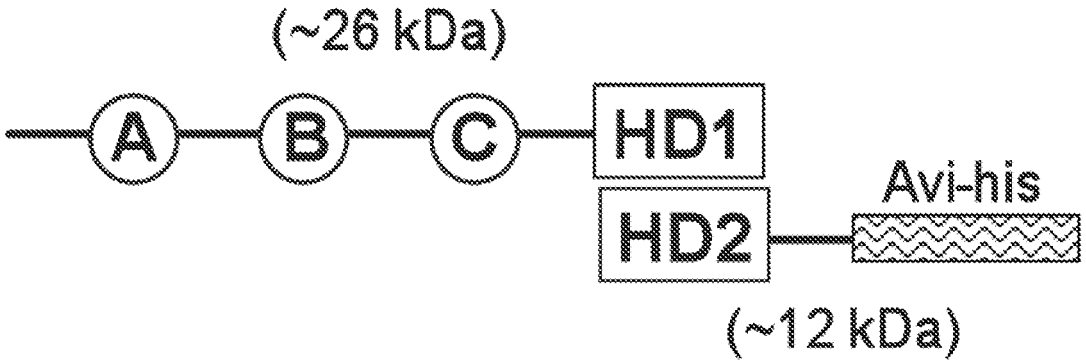
FIG. 1



Schematic diagram of recombinant Notch3 NRR protein immunogen with Avi- and his- tags.

FIG. 2

SEQ ID NO: 1 Human Notch3 NRR recombinant protein amino acid sequence

APEVSEEPRCPRAACQAKRGDQRCDRECNSPGCGWDGGDCSLSVGDPWRQCEALQCWRLFNNSRC
DPACSSPACLYDNFDCHAGGRERTCNPVYEKYCADHFADGRCDQGCNTEECGWDGLDCASEVPALLA
RGVLVLTVLLPPEELLRSSADFLQRLSAILRTSLRFRLDAHGQAMVFPYHRPSPGSEPRARRELAPEVIGS
VVMLEIDNRLCLQSPENDHCFPDAQSAADYLGALSAVERLDFPYPLRDVRGEPLEPPEPSVPgggsgggIndi
feaqkiewheggpphhhhhh

SEQ ID NO: 2 Human Notch3 NRR recombinant protein nucleotide sequence

GCACCCGAGGTCTCGGAGGAGCCGCGGTGCCCGCGCGCCGCCTGCCAGGCCAAGCGCGGGGACC
AGCGCTGCGACCGCGAGTGCAACAGCCCAGGCTGCGGCTGGGACGGCGGCGACTGCTCGCTGAG
CGTGGGCGACCCCTGGCGGCAATGCGAGGCGCTGCAGTGCTGGCGCCTCTTCAACAACAGCCGCT
GCGACCCCGCCTGCAGCTCGCCCGCCTGCCTCTACGACAACTTCGACTGCCACGCCGGTGGCCGC
GAGCGCACTTGCAACCCGGTGTACGAGAAGTACTGCGCCGACCACTTTGCCGACGGCCGCTGCGA
CCAGGGCTGCAACACGGAGGAGTGCGGCTGGGATGGGCTGGATTGTGCCAGCGAGGTGCCGGCC
CTGCTGGCCCGCGGCGTGCTGGTGCTCACAGTGCTGCTGCCGCCGGAGGAGCTACTGCGTTCCAG
CGCCGACTTTCTGCAGCGGCTCAGCGCCATCCTGCGCACCTCGCTGCGCTTCCGCCTGGACGCGC
ACGGCCAGGCCATGGTCTTCCCTTACCACCGGCCTAGTCCTGGCTCCGAACCCCGGGCCCGTCGG
GAGCTGGCCCCCGAGGTGATCGGCTCGGTAGTAATGCTGGAGATTGACAACCGGCTCTGCCTGCA
GTCGCCTGAGAATGATCACTGCTTCCCCGATGCCCAGAGCGCCGCTGACTACCTGGGAGCGTTGTC
AGCGGTGGAGCGCCTGGACTTCCCGTACCCACTGCGGGACGTGCGGGGGGGAGCCGCTGGAGCCT
CCAGAACCCAGCGTCCCGggaggggaagcggaggcggactgaacgacatcttcgaggctcagaaaatcgaatggcacgaaggt
ggcccaccacatcatcatcatcatcac

SEQ ID NO: 3 Mouse Notch3 NRR recombinant protein amino acid sequence

APEVPEEPRCPRAACQAKRGDQNCDRECNTPGCGWDGGDCSLNVDDPWRQCEALQCWRLFNNSRC
DPACSSPACLYDNFDCYSGGRDRTCNPVYEKYCADHFADGRCDQGCNTEECGWDGLDCASEVPALLA
RGVLVLTVLLPPEELLRSSADFLQRLSAILRTSLRFRLDARGQAMVFPYHRPSPGSESRVRRELGPEVIG
SVVMLEIDNRLCLQSAENDHCFPDAQSAADYLGALSAVERLDFPYPLRDVRGEPLEAPEQSVPgggsgggI
ndifeaqkiewheggpphhhhhh

SEQ ID NO: 4 Mouse Notch3 NRR recombinant protein nucleotide sequence

GCCCCTGAGGTCCCCGAGGAGCCACGGTGCCCGCGAGCGGCTTGCCAGGCCAAGCGAGGGGACC
AGAACTGCGATCGTGAGTGCAACACCCCAGGCTGTGGCTGGGATGGCGGTGACTGCTCACTGAAC
GTGGACGACCCCTGGAGGCAGTGTGAGGCACTGCAGTGCTGGCGTCTCTTCAACAACAGCCGGTG
TGACCCGGCCTGCAGCTCTCCAGCCTGCCTCTATGACAACTTTGACTGCTACTCTGGTGGCCGCGA
CCGCACCTGCAACCCTGTTTATGAGAAGTACTGCGCCGACCACTTTGCAGATGGCCGTTGTGACCA
GGGCTGCAACACTGAGGAATGCGGCTGGGATGGGCTGGACTGTGCCAGCGAGGTCCCGGCCCTTT
TGGCCCGAGGGGTTCTGGTCCTCACAGTTCTTCTGCCTCCTGAAGAGTTGCTGCGCTCCAGTGCCG
ACTTTCTGCAGCGACTCAGCGCTATTCTGCGCACCTCACTGCGCTTCCGCTTGGACGCACGTGGCC
AGGCCATGGTCTTCCCCTATCACCGGCCAAGCCCTGGCTCTGAATCCCGGGTCCGTCGTGAGCTGG
GTCCTGAGGTGATCGGCTCTGTGGTGATGCTGGAGATTGACAACCGGCTCTGTCTGCAGTCAGCTG
AGAATGACCACTGCTTCCCTGATGCCCAGAGTGCTGCTGACTACCTGGGAGCCTTGTCAGCAGTGG
AGCGACTTGATTTCCCATACCCACTTCGGGATGTGCGAGGAGAGCCGCTGGAGGCCCCAGAGCAGA
GCGTGCCAggaggggaagcggaggcggactgaacgacatcttcgaggctcagaaaatcgaatggcacgaaggtggcccaccacatca
tcatcatcatcac

FIG. 3

SEQ ID NO: 5 r28 VH amino acid sequence (CDRs underlined)
EVQLVESGGGLVQPGRSLTLSCVASGFTFRDYGMTWIRQAPGKGLTWVAYISSGSNYIYYAEAVKGRFTI
SRDNAKNTLYLQMTSLRSEDTALYFCTRRGPFVLDAWGQGASVTVSS

SEQ ID NO: 6 r28 VH nucleotide sequence
GAGGTGCAACTGGTGGAGTCTGGAGGAGGCTTAGTGCAGCCTGGAAGGTCCCTGACACTCTCCTGT
GTAGCCTCTGGATTCACTTTCAGGGACTATGGAATGACCTGGATTCGCCAGGCTCCAGGGAAGGGG
CTGACATGGGTTGCATATATTAGTAGTGGTAGCAATTACATCTATTATGCAGAAGCGGTGAAGGGCC
GATTCACCATCTCCAGAGACAATGCCAAGAACACCCTGTACCTGCAAATGACCAGTCTGAGGTCTGA
AGACACTGCCTTGTATTTTTGTACAAGACGAGGCCCGTTTGTTTTGGATGCCTGGGGTCAAGGAGCT
TCAGTCACTGTCTCCTCA

SEQ ID NO: 7 r28 VL amino acid sequence (CDRs underlined)
DIQMTQSPSFLSASVGDRVTINCKASQSINRYLHWFQQKLGEAPKLLIYNANGLQTGIPSRFSGSGSGTD
FTLTISSLQSEDVATYFCLQHNTWPDTFGAGTKLELK

SEQ ID NO: 8 r28 VL nucleotide sequence
GACATCCAGATGACCCAGTCTCCTTCATTCCTGTCTGCATCTGTGGGAGACAGAGTCACTATCAACT
GCAAAGCAAGTCAGAGTATTAACAGGTACTTACACTGGTTTCAGCAGAAACTTGGAGAAGCTCCCAA
ACTCCTGATATATAATGCAAACGGTTTGCAAACGGGCATCCCATCAAGGTTCAGTGGCAGTGGATCT
GGTACTGATTTCACACTTACCATCAGCAGCCTGCAGTCTGAAGATGTTGCCACATATTTCTGCTTGCA
GCATAATACGTGGCCGGACACGTTTGGCGCTGGGACCAAGCTGGAACTGAA

SEQ ID NO: 9 r75 VH amino acid sequence (CDRs underlined)
QVKLLQSGAALVKPGASVKMSCKASGYAFTDYWVTWVKQSHGKSLEWIGEISPNSGGTNFNEKFKGKA
TLTVDKSTSTAYMELSRLTSEDSAIYYCTRGEIRYNWFAYWGQGTLVTVSS

SEQ ID NO: 10 r75 VH nucleotide sequence
CAGGTCAAGCTGCTGCAGTCTGGGGCTGCACTGGTGAAGCCTGGAGCCTCTGTGAAGATGTCTTGC
AAAGCTTCTGGTTATGCATTCACTGACTACTGGGTGACCTGGGTGAAGCAGAGTCATGGAAAGAGCC
TTGAGTGGATTGGGGAAATTTCTCCTAACAGTGGTGGTACTAACTTCAATGAAAAGTTCAAGGGCAA
GGCCACATTGACTGTAGACAAATCCACCAGCACAGCCTATATGGAGCTCAGCAGATTGACATCTGAG
GACTCTGCAATCTATTACTGTACAAGAGGGGAAATCCGTTACAATTGGTTTGCTTACTGGGGCCAAG
GCACTCTGGTCACTGTCTCCTCA

SEQ ID NO: 11 r75 VL amino acid sequence (CDRs underlined)
DIQMTQSPSSLSASVGDRVTITCKASQNVGNNIAWYQQKPGKAPKLLIYYASNRYTGVPSRFSGSGYGT
DFTLTISSLQPEDFATYYCQRLYNSPFTFGGGTKVEIK

SEQ ID NO: 12 r75 VL nucleotide sequence
AACATTGTGATGACCCAGTCTCCCAAATCCATGTCCATATCAGTAGGAGACAGGGTCACCATGAACT
GCAAGGCCAGTCAGAATGTGGGTAATAATATAGCCTGGTATCAACAGAAACCAGGGCAGTCTCCTAA
ACTGTTGATCTACTATGCATCTAACCGGTACACTGGGGTCCCTGATCGCTTCACAGGCGGTGGATAT
GGGACAGATTTCACTCTCACCATCAATAGTATGCAAGCTGAAGATGCAGCCTTTTATTACTGTCAGCG
TCTTTACAATTCTCCATTCACGTTCGGCTCAGGGACGAAGTTGGAAATAAAG

FIG. 4A

SEQ ID NO: 13 hu28 VH 1.0 amino acid sequence
EVQLVESGGGLVQPGGSLRLSCAASGFTFRDYGMTWVRQAPGKGLEWVAYISSGSNYIYYAEAVKGRF
TISRDNAKNSLYLQMNSLRAEDTAVYYCARRGPFVLDAWGQGTLVTVSS

SEQ ID NO: 14 hu28 VH 1.0 nucleotide sequence
GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTG
TGCAGCCTCTGGATTCACTTTCAGGGACTATGGAATGACCTGGGTCCGCCAGGCTCCAGGGAAGGG
GCTGGAGTGGGTGGCCTATATTAGTAGTGGTAGCAATTACATCTATTATGCAGAAGCGGTGAAGGGC
CGATTCACCATCTCCAGAGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG
AGGACACGGCTGTGTATTACTGTGCGAGACGAGGCCCGTTTGTTTTGGATGCCTGGGGCCAGGGAA
CCCTGGTCACCGTCTCCTCA

SEQ ID NO: 15 hu28 VH 1.0 CDR1 amino acid sequence-Kabat
DYGMT

SEQ ID NO: 16 hu28 VH 1.0 CDR1 amino acid sequence-Chothia
GFTFRDY

SEQ ID NO: 17 hu28 VH 1.0 CDR1 nucleotide sequence-Kabat
GACTATGGAATGACC

SEQ ID NO: 18 hu28 VH 1.0 CDR1 nucleotide sequence-Chothia
GGATTCACTTTCAGGGACTAT

SEQ ID NO: 19 hu28 VH 1.0 CDR2 amino acid sequence-Kabat
YISSGSNYIYYAEAVKG

SEQ ID NO: 20 hu28 VH 1.0 CDR2 amino acid sequence-Chothia
SSGSNY

SEQ ID NO: 21 hu28 VH 1.0 CDR2 nucleotide sequence-Kabat
TATATTAGTAGTGGTAGCAATTACATCTATTATGCAGAAGCGGTGAAGGGC

SEQ ID NO: 22 hu28 VH 1.0 CDR2 nucleotide sequence-Chothia
AGTAGTGGTAGCAATTAC

SEQ ID NO: 23 hu28 VH 1.0 CDR3 amino acid sequence-Kabat and Chothia
RGPFVLDA

SEQ ID NO: 24 hu28 VH 1.0 CDR3 nucleotide sequence-Kabat and Chothia
CGAGGCCCGTTTGTTTTGGATGCC

FIG. 4B

SEQ ID NO: 25 hu28 VL 1.0 amino acid sequence
DIQMTQSPSSLSASVGDRVTITCKASQSINRYLHWYQQKPGKAPKLLIYNANGLQTGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCLQHNTWPDTFGGGTKVEIK

SEQ ID NO: 26 hu28 VL 1.0 nucleotide sequence
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTT
GCAAAGCAAGTCAGAGTATTAACAGGTACTTACACTGGTATCAGCAGAAACCAGGGAAAGCCCCTAA
GCTCCTGATCTATAATGCAAACGGTTTGCAAACGGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCT
GGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTTTGCA
GCATAATACGTGGCCGGACACGTTTGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 27 hu28 VL 1.0 CDR1 amino acid sequence-Kabat and Chothia
KASQSINRYLH

SEQ ID NO: 28 hu28 VL 1.0 CDR1 nucleotide sequence-Kabat and Chothia
AAAGCAAGTCAGAGTATTAACAGGTACTTACAC

SEQ ID NO: 29 hu28 VL 1.0 CDR2 amino acid sequence-Kabat and Chothia
NANGLQT

SEQ ID NO: 30 hu28 VL 1.0 CDR2 nucleotide sequence-Kabat and Chothia
AATGCAAACGGTTTGCAAACG

SEQ ID NO: 31 hu28 VL 1.0 CDR3 amino acid sequence-Kabat and Chothia
LQHNTWPDT

SEQ ID NO: 32 hu28 VL 1.0 CDR3 nucleotide sequence-Kabat and Chothia
TTGCAGCATAATACGTGGCCGGACACGTTT

FIG. 4C

SEQ ID NO: 33 hu28 HC 1.0 amino acid sequence-Human IgG1

EVQLVESGGGLVQPGGSLRLSCAASGFTFRDYGMTWVRQAPGKGLEWVAYISSGSNYIYYAEAVKGRF
TISRDNAKNSLYLQMNSLRAEDTAVYYCARRGPFVLDAWGQGTLVTVSSASTKGPSVFPLAPSSKSTSG
GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW
YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPG

SEQ ID NO: 34 hu28 HC 1.0 nucleotide sequence

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTG
TGCAGCCTCTGGATTCACTTTCAGGGACTATGGAATGACCTGGGTCCGCCAGGCTCCAGGGAAGGG
GCTGGAGTGGGTGGCCTATATTAGTAGTGGTAGCAATTACATCTATTATGCAGAAGCGGTGAAGGGC
CGATTCACCATCTCCAGAGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG
AGGACACGGCTGTGTATTACTGTGCGAGACGAGGCCCGTTTGTTTTGGATGCCTGGGGCCAGGGAA
CCCTGGTCACCGTCTCCTCAGCGTCGACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCA
AGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG
ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTC
CTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTA
CATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCTTGT
GACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTC
TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG
GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAAT
GCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGT
CCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGC
CCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCC
CCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCC
CAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTC
CCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGC
AGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGA
GCCTCTCCCTGTCCCCGGGT

SEQ ID NO: 35 hu28 LC 1.0 amino acid sequence-Human kappa

DIQMTQSPSSLSASVGDRVTITCKASQSINRYLHWYQQKPGKAPKLLIYNANGLQTGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCLQHNTWPDTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP
REAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN
RGEC

SEQ ID NO: 36 hu28 LC 1.0 nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTT
GCAAAGCAAGTCAGAGTATTAACAGGTACTTACACTGGTATCAGCAGAAACCAGGGAAAGCCCCTAA
GCTCCTGATCTATAATGCAAACGGTTTGCAAACGGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCT
GGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTTTGCA
GCATAATACGTGGCCGGACACGTTTGGCGGAGGGACCAAGGTGGAGATCAAA
CGGACCGTGGCCGCTCCTTCCGTGTTCATCTTCCCCCCTTCCGACGAGCAGCTGAAGTCTGGCACC
GCCTCTGTGGTGTGTCTGCTGAACAACTTCTACCCCCGGGAGGCCAAGGTGCAGTGGAAGGTGGAC
AACGCTCTGCAGTCCGGCAACTCCCAGGAGTCTGTGACCGAGCAGGACTCCAAGGACAGCACCTAC
TCCCTGTCCTCTACCCTGACCCTGTCCAAGGCCGACTACGAGAAGCACAAGGTGTACGCCTGTGAG
GTGACCCACCAGGGCCTGTCCTCTCCTGTGACCAAGTCCTTCAACCGGGGCGAGTGC

FIG. 5A

SEQ ID NO: 37 hu75 VH 1.9 amino acid sequence
EVQLVESGGGLVQPGGSLRLSCAASGYAFTDYWMTWVRQAPGKGLEWVAEISPNSGGTNFNEKFKGR
FTISVDNAKNSLYLQMNSLRAEDTAVYYCARGEIRYNWFAYWGQGTLVTVSS

SEQ ID NO: 38 hu75 VH 1.9 nucleotide sequence
GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTG
TGCAGCCTCTGGTTATGCATTCACTGACTACTGGATGACCTGGGTCCGCCAGGCTCCAGGGAAGGG
GCTGGAGTGGGTGGCCGAAATTTCTCCTAACAGTGGTGGTACTAACTTCAATGAAAAGTTCAAGGGC
CGATTCACCATCTCCGTTGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG
AGGACACGGCTGTGTATTACTGTGCGAGAGGGGAAATCCGTTACAATTGGTTTGCTTACTGGGGCCA
GGGAACCCTGGTCACCGTCTCCTCA

SEQ ID NO: 39 hu75 VH 1.9 CDR1 amino acid sequence-Kabat
DYWMT

SEQ ID NO: 40 hu75 VH 1.9 CDR1 amino acid sequence-Chothia
GYAFTDY

SEQ ID NO: 41 hu75 VH 1.9 CDR1 nucleotide sequence-Kabat
GACTACTGGATGACC

SEQ ID NO: 42 hu75 VH 1.9 CDR1 nucleotide sequence-Chothia
GGTTATGCATTCACTGACTAC

SEQ ID NO: 43 hu75 VH 1.9 CDR2 amino acid sequence-Kabat
EISPNSGGTNFNEKFKG

SEQ ID NO: 44 hu75 VH 1.9 CDR2 amino acid sequence-Chothia
SPNSGG

SEQ ID NO: 45 hu75 VH 1.9 CDR2 nucleotide sequence-Kabat
GAAATTTCTCCTAACAGTGGTGGTACTAACTTCAATGAAAAGTTCAAGGGC

SEQ ID NO: 46 hu75 VH 1.9 CDR2 nucleotide sequence-Chothia
TCTCCTAACAGTGGTGGT

SEQ ID NO: 47 hu75 VH 1.9 CDR3 amino acid sequence-Kabat and Chothia
GEIRYNWFAY

SEQ ID NO: 48 hu75 VH 1.9 CDR3 nucleotide sequence-Kabat and Chothia
GGGGAAATCCGTTACAATTGGTTTGCTTAC

FIG. 5B

SEQ ID NO: 49 hu75 VL 1.3 amino acid sequence
DIQMTQSPSSLSASVGDRVTITCKASQNVGNNIAWYQQKPGKAPKLLIYYASNRYTGVPSRFSGSGYGT
DFTLTISSLQPEDFATYYCQRLYNSPFTFGGGTKVEIK

SEQ ID NO: 50 hu75 VL 1.3 nucleotide sequence
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTT
GCAAGGCCAGTCAGAATGTGGGTAATAATATAGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTA
AGCTCCTGATCTATTATGCATCTAACCGGTACACTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATA
TGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAGC
GTCTTTACAATTCTCCATTCACGTTCGGCGGAGGGACCAAGGTGGAGATCAAA

SEQ ID NO: 51 hu75 VL 1.3 CDR1 amino acid sequence-Kabat and Chothia
KASQNVGNNIA

SEQ ID NO: 52 hu75 VL 1.3 CDR1 nucleotide sequence-Kabat and Chothia
AAGGCCAGTCAGAATGTGGGTAATAATATAGCC

SEQ ID NO: 53 hu75 VL 1.3 CDR2 amino acid sequence-Kabat and Chothia
YASNRYT

SEQ ID NO: 54 hu75 VL 1.3 CDR2 nucleotide sequence-Kabat and Chothia
TATGCATCTAACCGGTACACT

SEQ ID NO: 55 hu75 VL 1.3 CDR3 amino acid sequence-Kabat and Chothia
QRLYNSPFT

SEQ ID NO: 56 hu75 VL 1.3 CDR3 nucleotide sequence-Kabat and Chothia
CAGCGTCTTTACAATTCTCCATTCACGTTC

FIG. 5C

SEQ ID NO: 57 hu75 HC 1.9 amino acid sequence-Human IgG1

EVQLVESGGGLVQPGGSLRLSCAASGYAFTDYWMTWVRQAPGKGLEWVAEISPNSGGTNFNEKFKGR
FTISVDNAKNSLYLQMNSLRAEDTAVYYCARGEIRYNWFAYWGQGTLVTVSSASTKGPSVFPLAPSSKST
SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHK
PSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF
NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPR
EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG

SEQ ID NO: 58 hu75 HC 1.9 nucleotide sequence

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTG
TGCAGCCTCTGGTTATGCATTCACTGACTACTGGATGACCTGGGTCCGCCAGGCTCCAGGGAAGGG
GCTGGAGTGGGTGGCCGAAATTTCTCCTAACAGTGGTGGTACTAACTTCAATGAAAAGTTCAAGGGC
CGATTCACCATCTCCGTTGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG
AGGACACGGCTGTGTATTACTGTGCGAGAGGGGAAATCCGTTACAATTGGTTTGCTTACTGGGGCCA
GGGAACCCTGGTCACCGTCTCCTCAGCGTCGACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTC
CTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAAC
CGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTA
CAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAG
ACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAAT
CTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCT
TCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGG
TGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTG
CATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTC
ACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTC
CCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACC
CTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTC
TATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCAC
GCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAG
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GAAGAGCCTCTCCCTGTCCCCGGGT

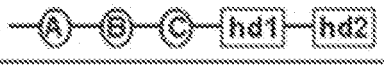
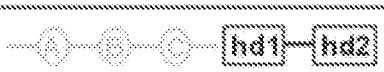
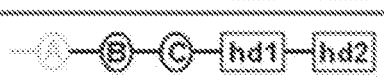
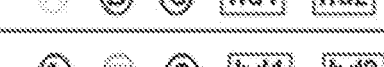
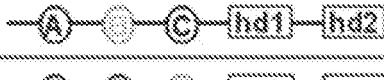
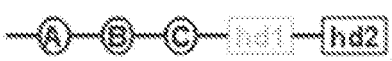
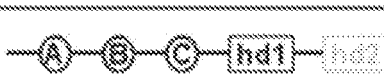
SEQ ID NO: 59 hu75 LC 1.3 amino acid sequence-Human kappa

DIQMTQSPSSLSASVGDRVTITCKASQNVGNNIAWYQQKPGKAPKLLIYYASNRYTGVPSRFSGSGYGT
DFTLTISSLQPEDFATYYCQRLYNSPFTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP
REAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN
RGEC

SEQ ID NO: 60 hu28 LC 1.3 nucleotide sequence

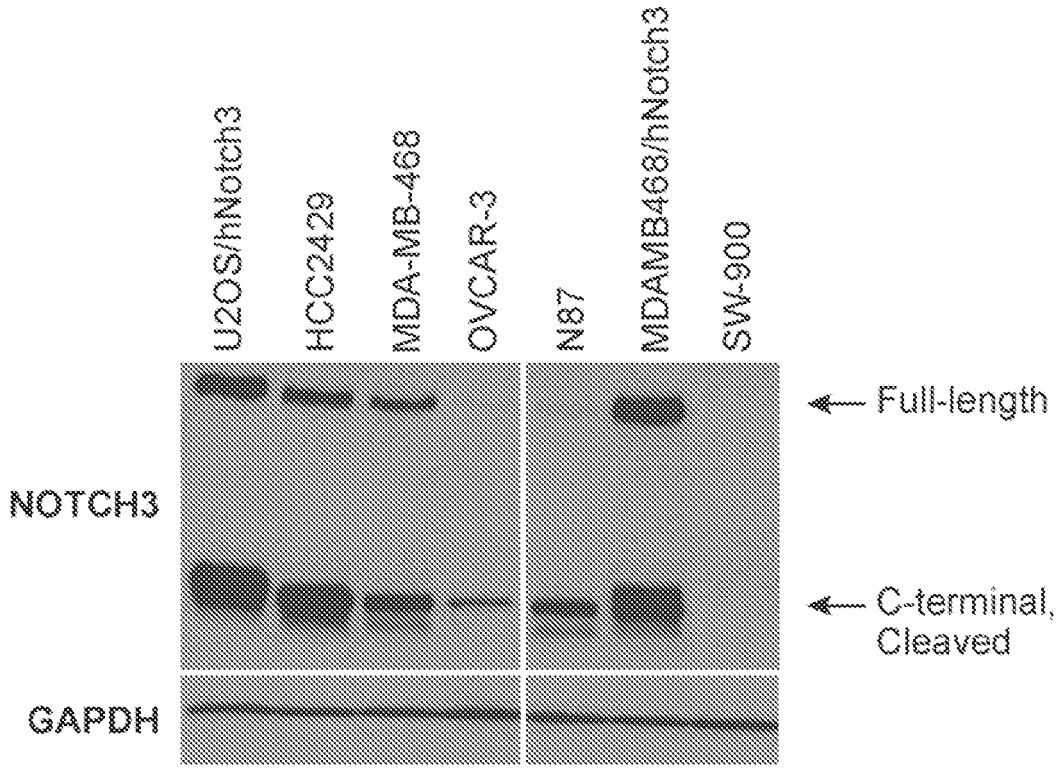
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTT
GCAAGGCCAGTCAGAATGTGGGTAATAATATAGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTA
AGCTCCTGATCTATTATGCATCTAACCGGTACACTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATA
TGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAGC
GTCTTTACAATTCTCCATTCACGTTCGGCGGAGGGACCAAGGTGGAGATCAAACGGACCGTGGCCG
CTCCTTCCGTGTTCATCTTCCCCCCTTCCGACGAGCAGCTGAAGTCTGGCACCGCCTCTGTGGTGTG
TCTGCTGAACAACTTCTACCCCCGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCTCTGCAGTC
CGGCAACTCCCAGGAGTCTGTGACCGAGCAGGACTCCAAGGACAGCACCTACTCCCTGTCCTCTAC
CCTGACCCTGTCCAAGGCCGACTACGAGAAGCACAAGGTGTACGCCTGTGAGGTGACCCACCAGG
GCCTGTCCTCTCCTGTGACCAAGTCCTTCAACCGGGGCGAGTGC

FIG. 6

antibody	ch28	ch75
Notch3-NRR 	2.06	1.72
Notch1-NRR 	-	-
	-	-
	0.15	-
	0.54	2.37
	-	0.80
	-	-
	0.5	-
	-	-

Recombinant human Notch1 NRR and Notch3 NRR domain swap chimeric constructs for epitope mapping of anti-Notch3 ch28 and ch75 antibodies.

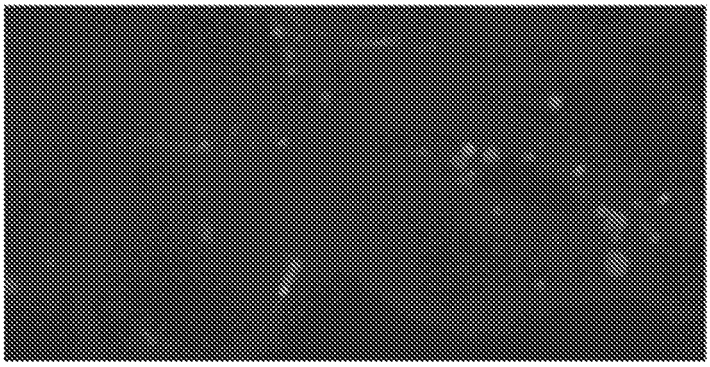
FIG. 7



Western blot analysis of Notch3 positive and negative cell lines using the D11B8 antibody.

FIG. 8A

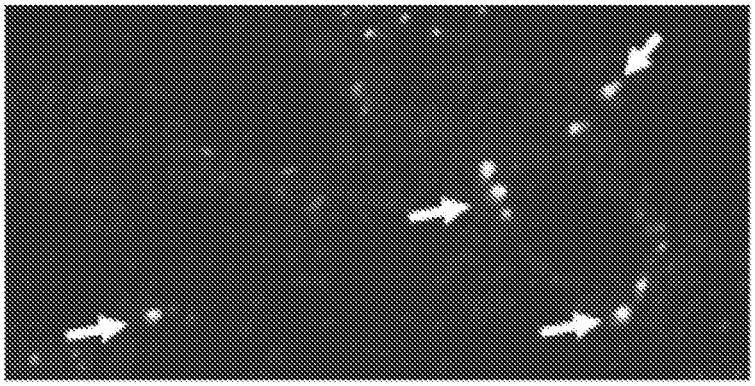
a) 0 hr



Cell membrane localization of anti-Notch3 antibody hu75-Alexa 488 and labeling of acidic vesicles with pHrodoTM red dextran in MDA-MB-468 breast cancer cells at hour 0.

FIG. 8B

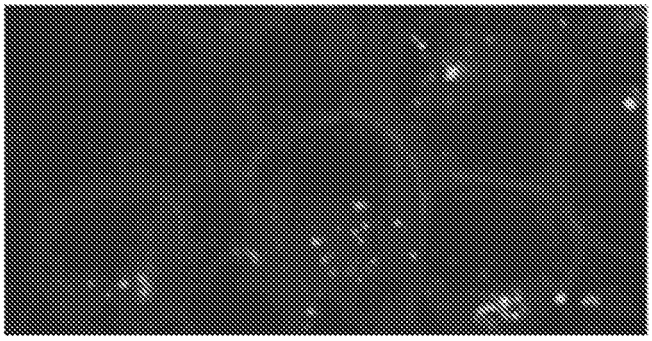
b) 5 hr



Intracellular trafficking of anti-Notch3 antibody hu75-Alexa 488 and co-localization with pHrodoTM red dextran in MDA-MB-468 breast cancer cells at hour 5 (arrows).

FIG. 8C

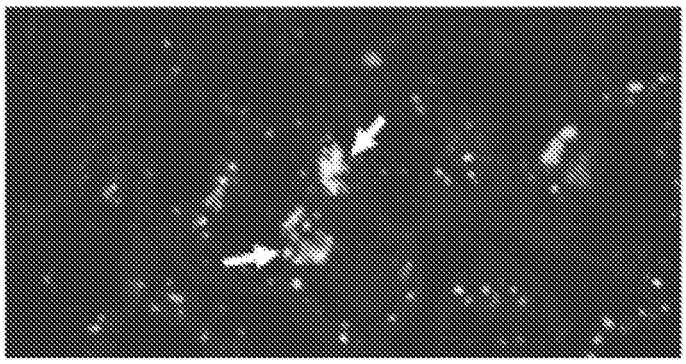
c) 0 hr



Cell membrane localization of anti-Notch3 antibody hu28-DyLight650 and labeling of acidic vesicles with pHrodoTM red dextran (intracellular puncta) in MDA-MB-468 breast cancer cells at hour 0.

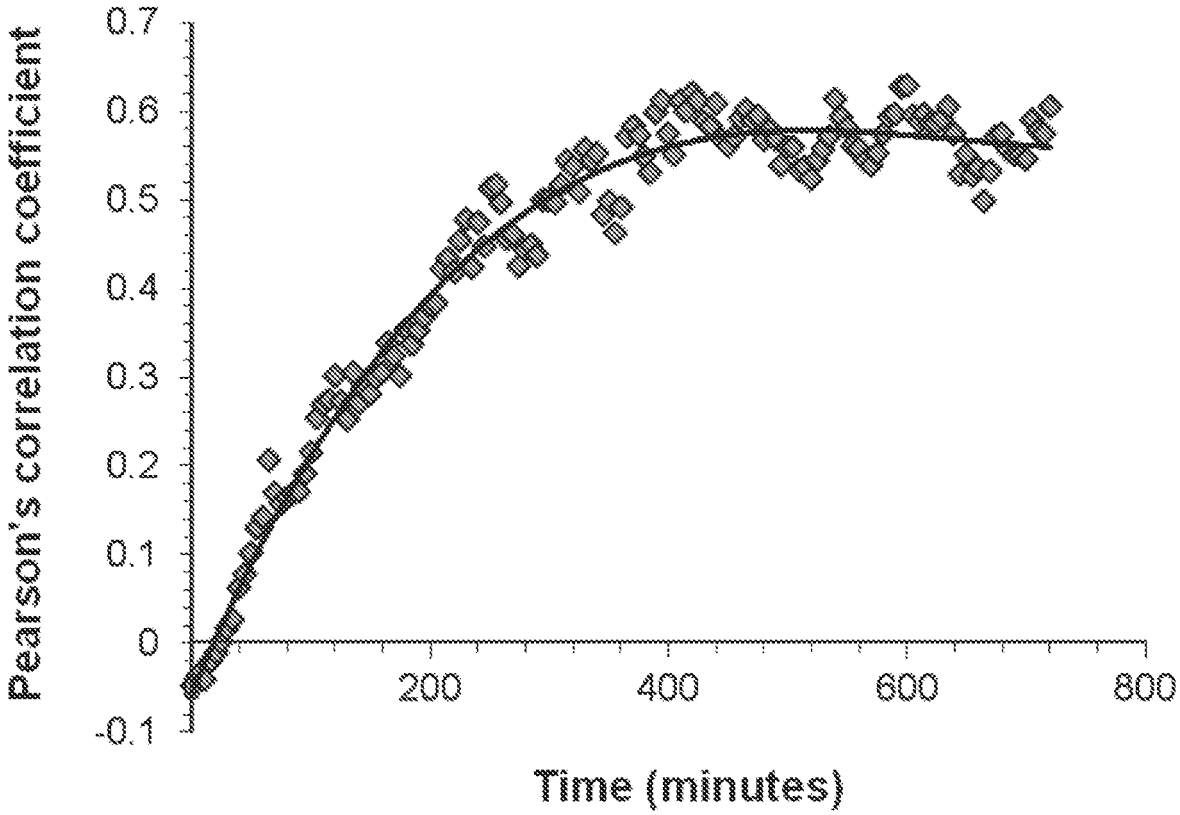
FIG. 8D

d) 8 hr



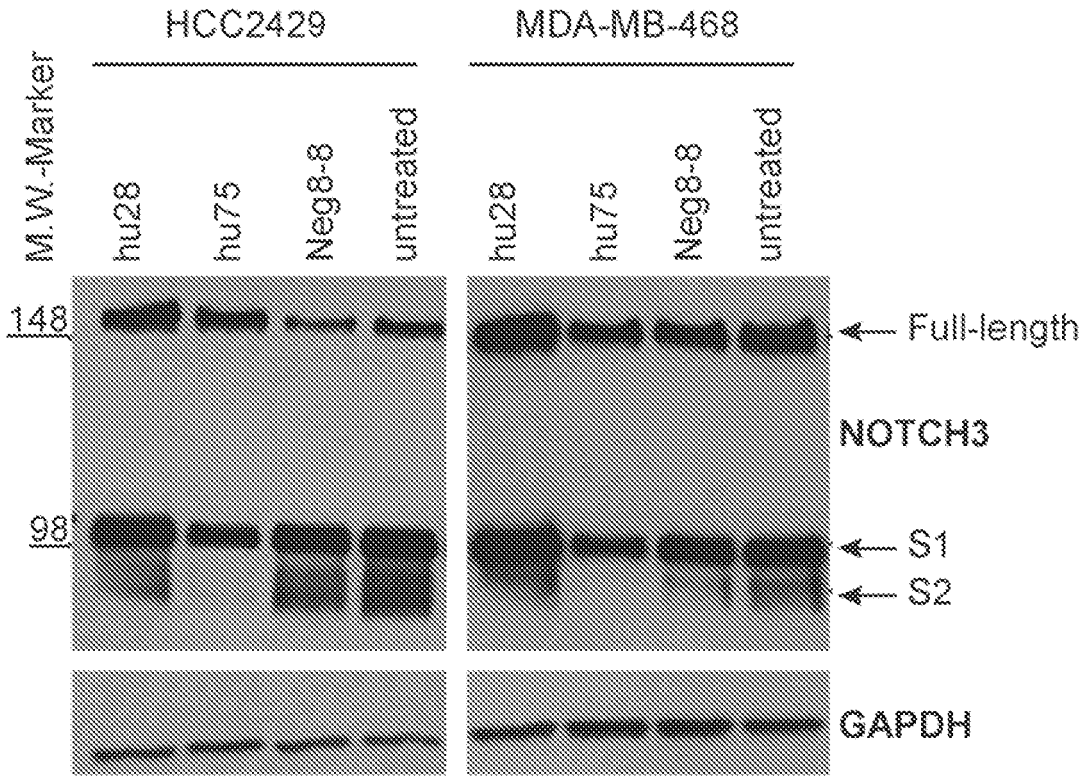
Intracellular trafficking of anti-Notch3 antibody hu28-DyLight650 and co-localization with pHrodoTM red dextran in MDA-MB-468 breast cancer cells at hour 8 (arrows).

FIG. 8E



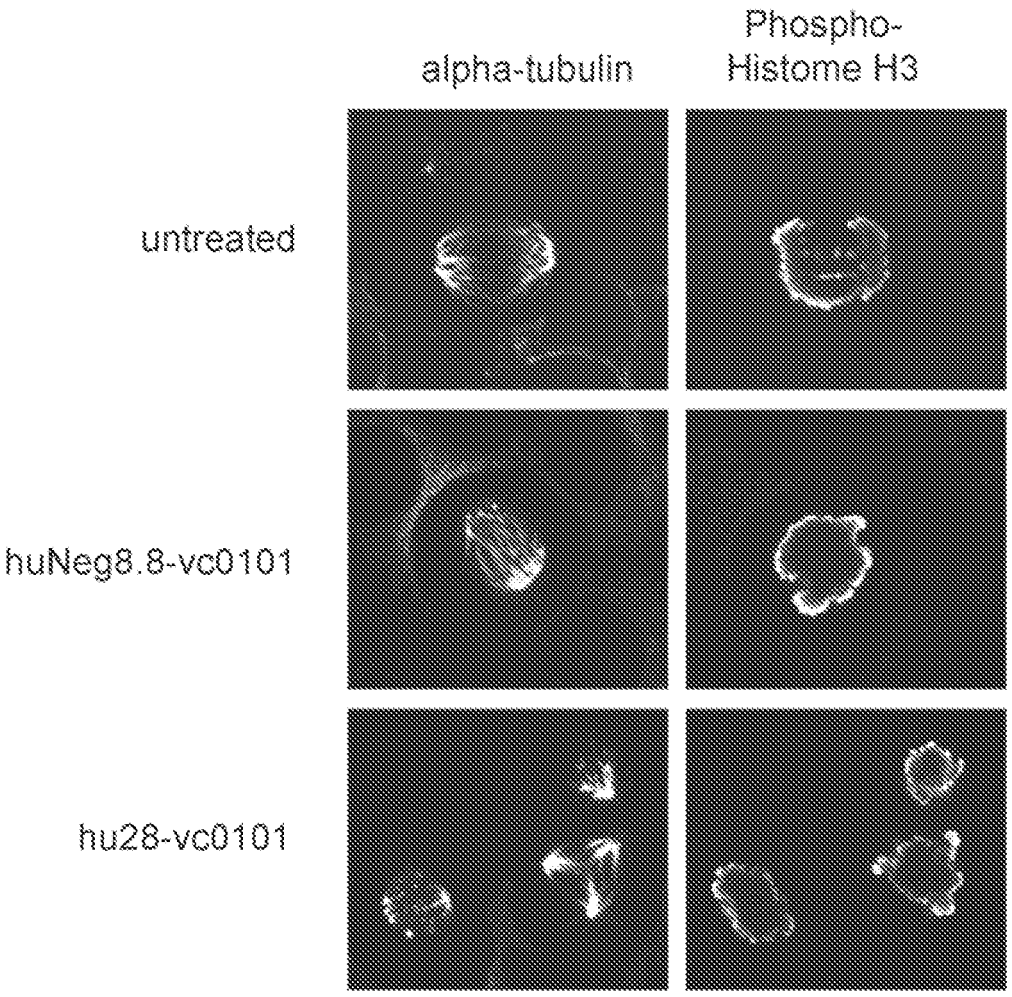
Pearson's correlation coefficient demonstrating the degree of overlap or co-localization of hu28-DyLight650 and pHrodoTM red dextran fluorescent labels in MDA-MB-468 cells over time.

FIG. 9



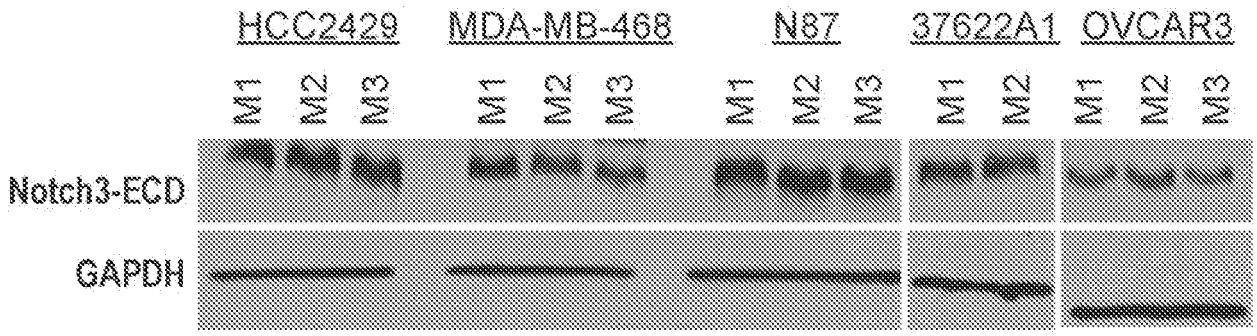
Western blot analysis of S2-cleavage assay using HCC2429 and MDA-MB-468 cells treated with humanized anti-Notch3 antibodies. M.W. = molecular weight.

FIG. 10



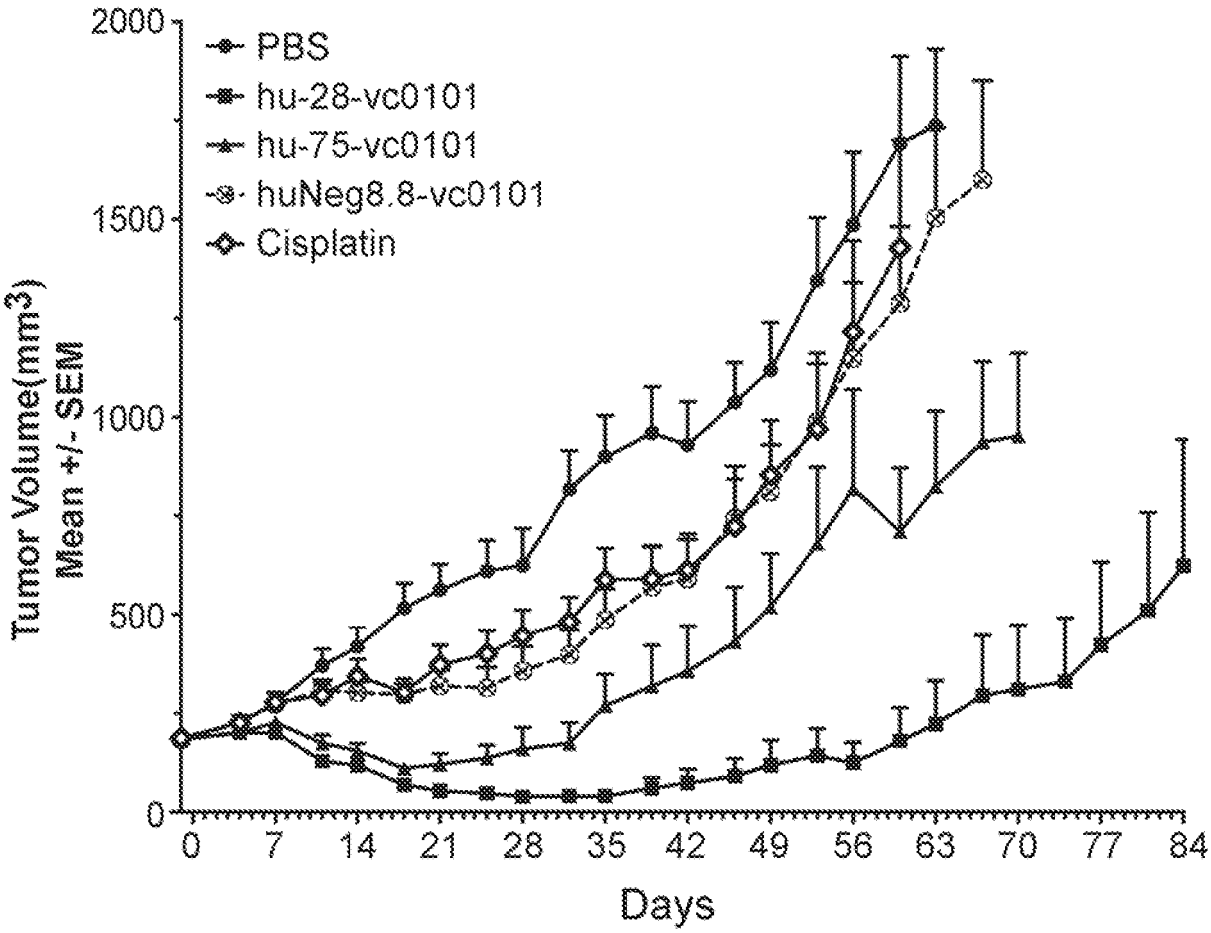
Treatment of OVCAR3 ovarian cancer cells with anti-Notch3 hu28-vc0101 disrupts microtubules (stained with anti-alpha-tubulin antibody) in mitotic cells that were identified by phospho-Histone H3 staining.

FIG. 11



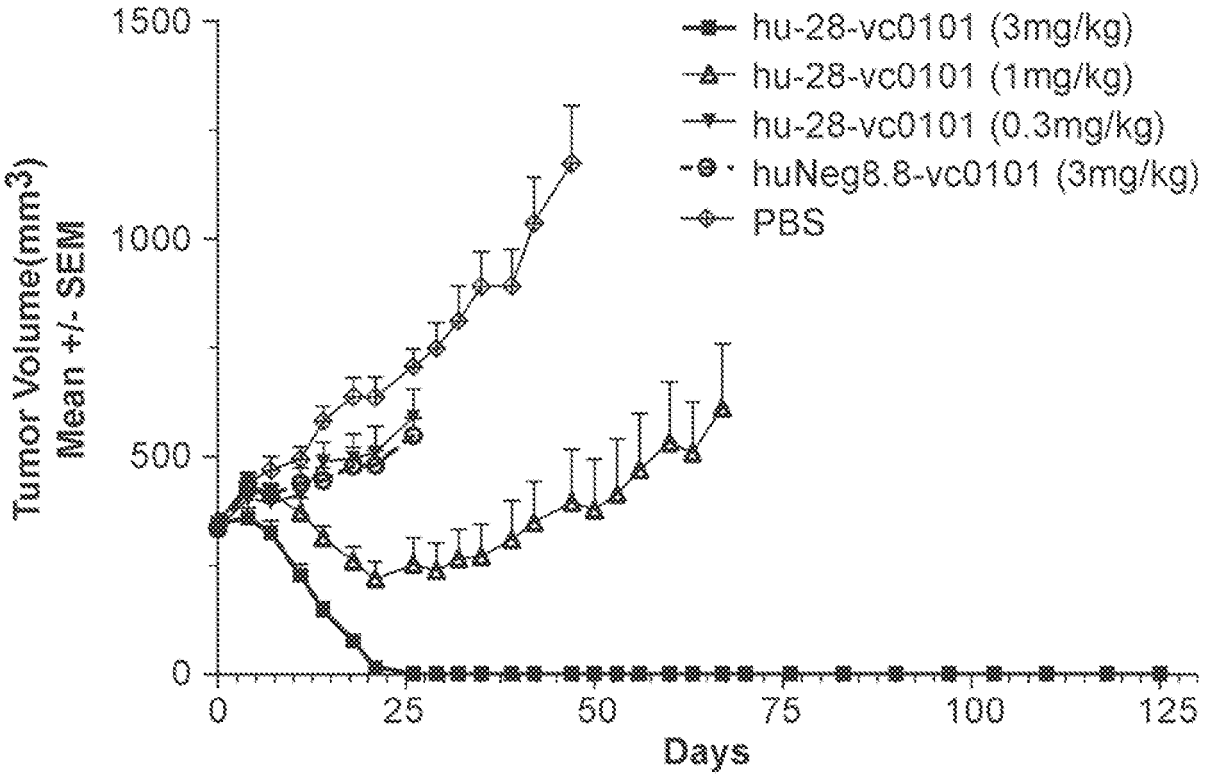
Western blot analysis of Notch3-ECD from xenografts harvested from 2-3 mice (M).

FIG. 12



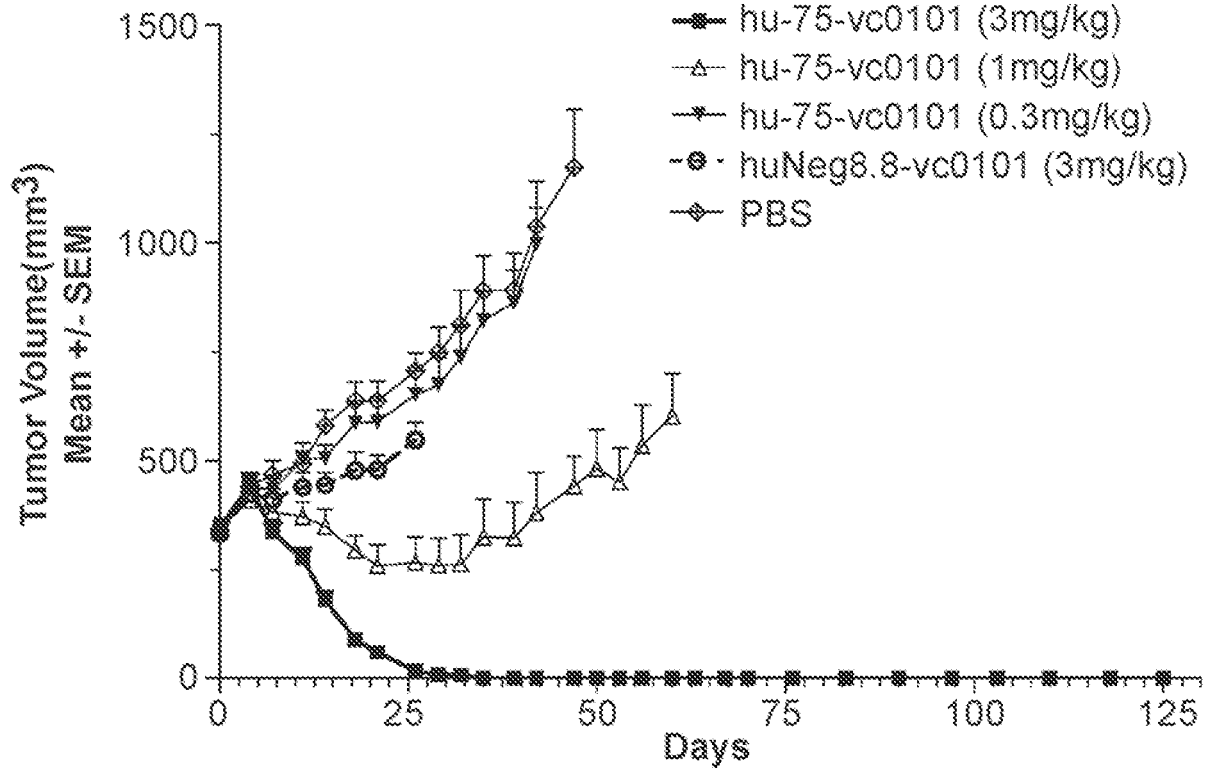
Efficacy of anti-Notch3 hu28-vc0101 and hu75-vc0101at a dose of 3 mg/kg compared to Cisplatin at a dose of at 5 mg/kg in the 37622A1 NSCLC patient derived xenografts model.

FIG. 13A



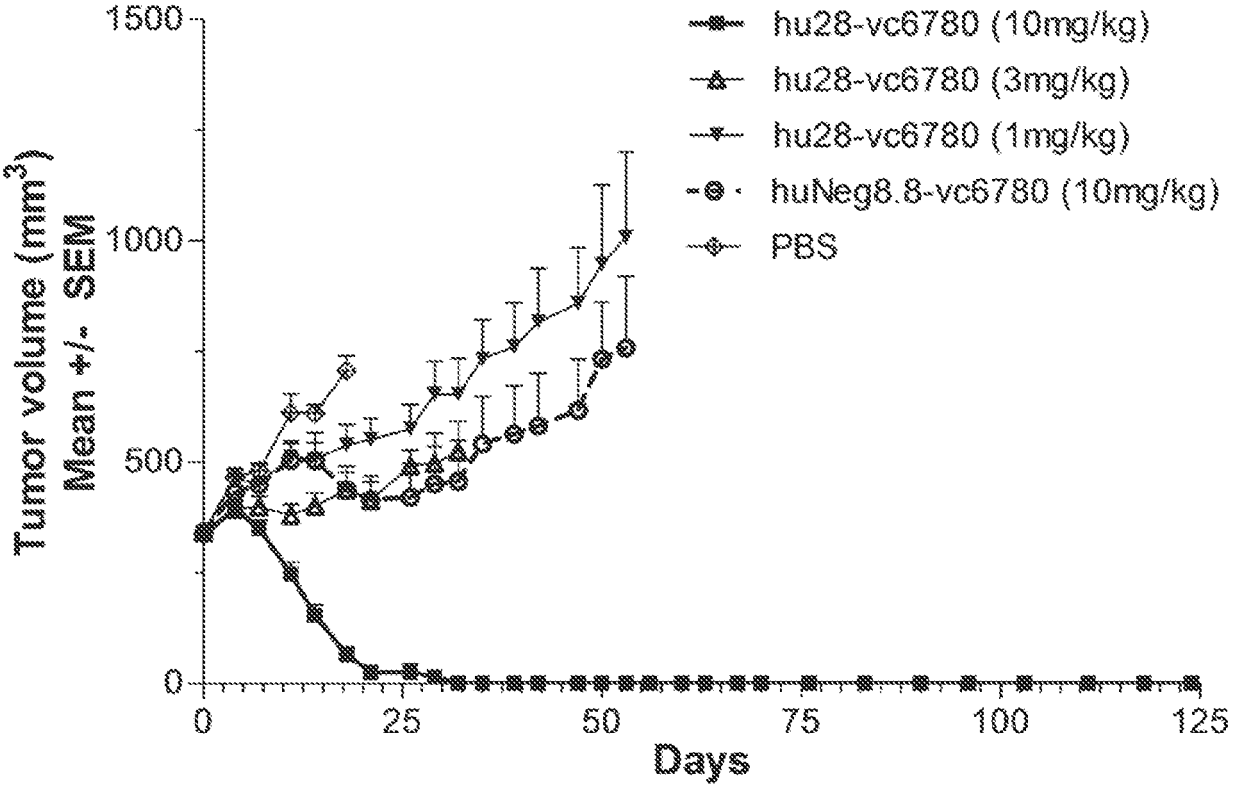
Efficacy of anti-Notch3 hu28-vc0101 in the MDA-MB-468 breast model.

FIG. 13B



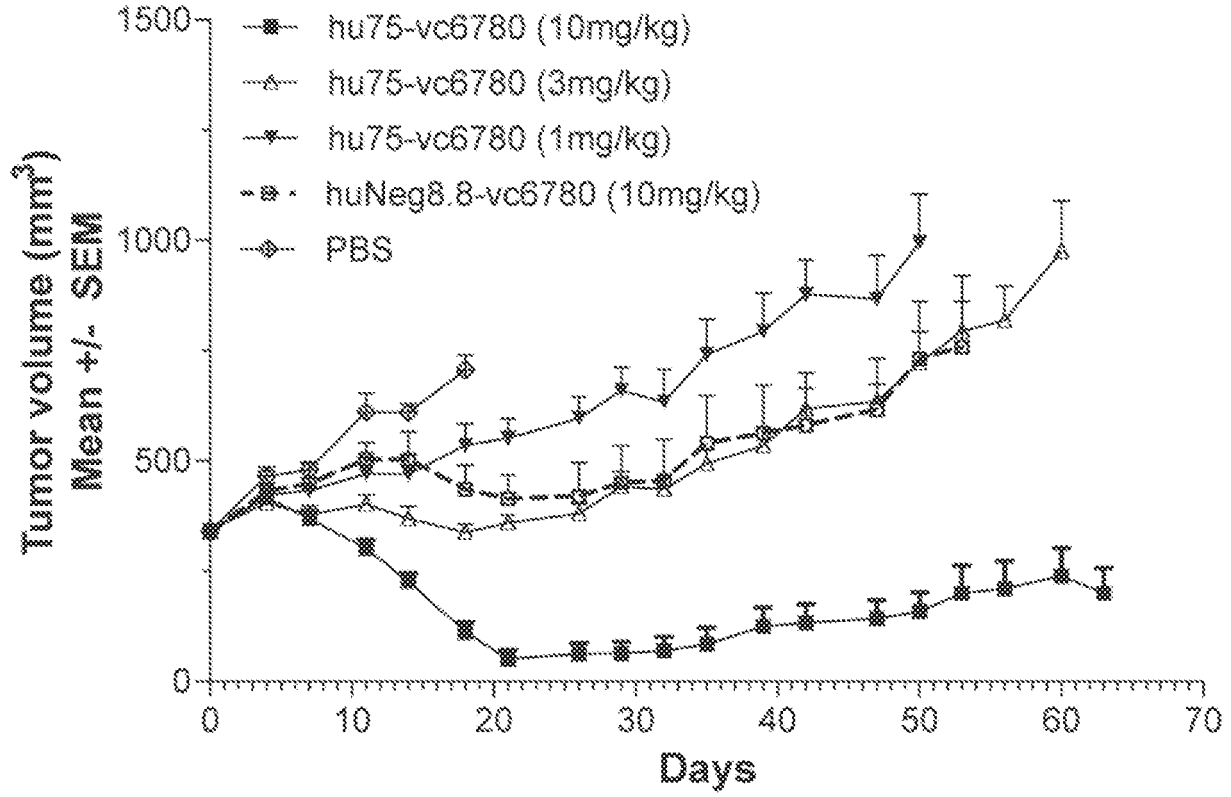
Efficacy of anti-Notch3 hu75-vc0101 in the MDA-MB-468 breast model.

FIG. 14A



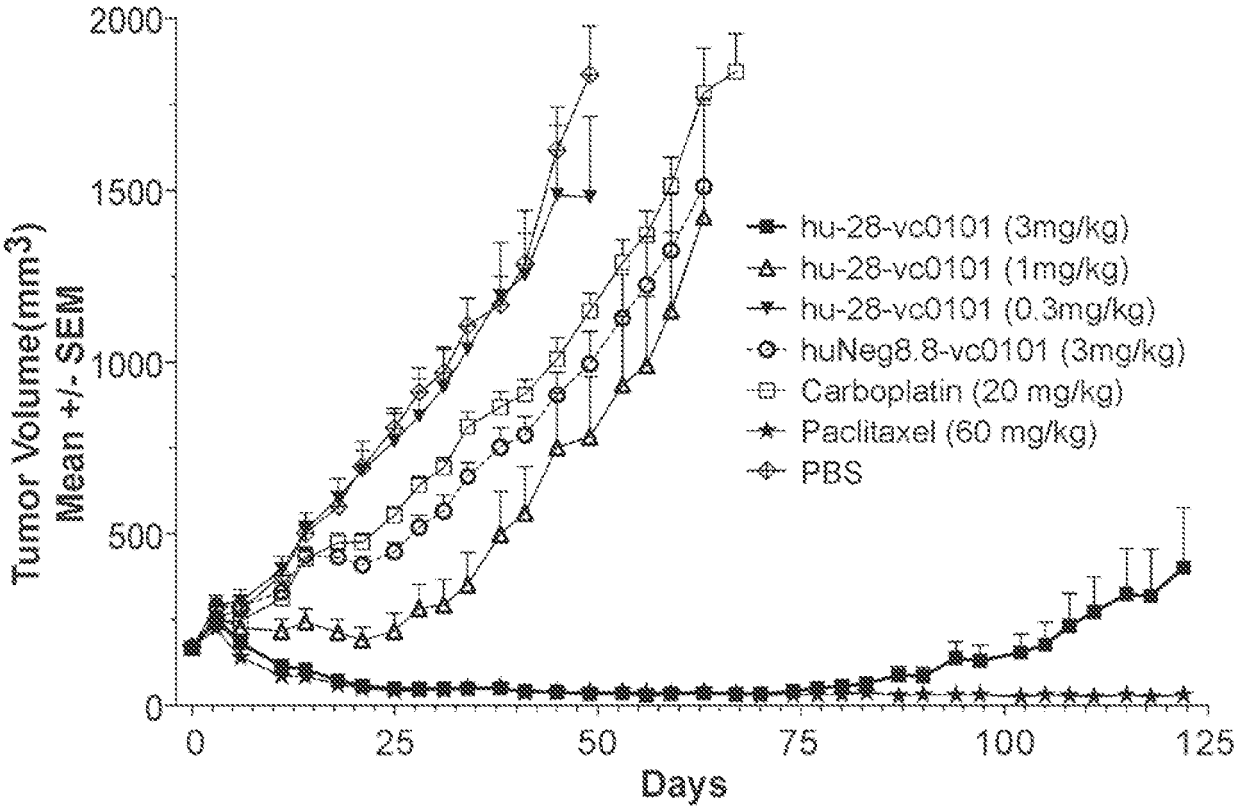
Efficacy of anti-Notch3 hu28-vc6780 in the MDA-MB-468 breast model.

FIG. 14B



Efficacy of anti-Notch3 hu75-vc6780 in the MDA-MB-468 breast model.

FIG. 15



Efficacy of anti-Notch3 hu28-vc0101 in the OVCAR3 ovarian model.

FIG. 16A Efficacy of rat-human chimeric anti-Notch3 ADCs dosed at 5mg/kg in HCC2429 lung xenografts

	HCC2429 Lung xenografts, tumor volume (mm^3 +/- SEM)														
Day	PBS	ch28-mc0101	ch28-mc3377	ch28-me0131	ch28-MALPEG6C2-0131	ch75-mc0131	ch28-vc0101	ch28-vc6780	ch75-vc0101	ch75-vc6780	huNeg8.8-mc0131	huNeg8.B-mc3377	huNeg8.B-me0131	huNeg8.8-vc0101	huNeg8.8-vc6780
-2	198 ±44	195 ±37	195 ±39	196 ±39	196 ±47	195 ±35	195 ±26	195 ±33	195 ±25	205 ±35	195 ±43	175 ±47	195 ±42	196 ±41	195 ±43
2	503 ±106	457 ±73	525 ±101	458 ±90	505 ±128	483 ±96	395 ±54	378 ±77	450 ±46	420 ±66	603 ±119	546 ±140	543 ±115	602 ±127	516 ±117
4	838 ±187	506 ±96	654 ±136	504 ±112	638 ±192	522 ±125	298 ±46	329 ±73	366 ±47	430 ±92	845 ±149	714 ±186	746 ±168	766 ±191	759 ±177
6	1008 ±229	562 ±126	789 ±156	600 ±152	750 ±207	634 ±158	259 ±33	319 ±79	318 ±48	474 108	1117 ±171	939 ±243	1016 ±225	1000 ±262	988 ±229
9	1618 ±265	652 ±133	1186 ±253	787 ±177	1020 ±213	620 ±129	177 ±24	280 ±72	217 ±30	502 ±125	1773 ±264	1346 ±284	1506 ±367	1372 ±385	1449 ±304
11	1605± 228	761 ±166	1458 ±314	941 ±199	1302 ±257	737 ±162	169 ±22	290 ±77	196 ±30	601 ±155	1986 ±170	1608 ±259	1475 ±283	1331 ±399	1582 ±316
13	2033± 293	865 ±176	1534 ±339	1096 ±264	1599 ±274	802 ±184	122 ±15	293 ±88	166 ±33	735 ±186	2535 ±228	2257 ±350	1831 ±400	-	-
16	-	917 ±207	-	949 ±190	1556 ±300	878 ±200	97 ±13	266 ±105	120 ±26	781 ±210	-	-	-	-	-
19	-	1222 ±275	-	1322 ±276	1966 ±414	1051 ±247	88 ±14	484 ±171	102 ±28	770 ±153	-	-	-	-	-
23		1694 ±401	-	-	-	1354 ±340	79 ±25	496 ±238	72 ±25	855 ±156	-	-	-	-	-
26	-	-	-	-	-	-	77 ±47	658 ±329	64 ±28	1159 ±253	-	-	-	-	-
30	-	-	-	-	-	-	109 ±86	533 ±290	36 ±20	1270 ±205	-	-	-	-	-
33	-	-	-	-	-	-	138 ±128	775 ±411	36 ±34	1628 ±309	-	-	-	-	-
37	-	-	-	-	-	-	210 ±199	-	46 ±45	-	-	-	-	-	-
40	-	-	-	-	-	-	323 ±311	-	58 ±57	-	-	-	-	-	-
44	-	-	-	-	-	-	17 ±17	-	108 ±107	-	-	-	-	-	-
51	-	-	-	-	-	-	43 ±43	-	201 ±200	-	-	-	-	-	-
58	-	-	-	-	-	-	82 ±82	-	0±0	-	-	-	-	-	-
65	-	-	-	-	-	-	138 ±138	-	0±0	-	-	-	-	-	-
73	-	-	-	-	-	-	301 ±301	-	0±0	-	-	-	-	-	-
79	-	-	-	-	-	-	-	-	0±0	-	-	-	-	-	-
89	-	-	-	-	-	-	-	-	0±0	-	-	-	-	-	-
96	-	-	-	-	-	-	-	-	0±0	-	-	-	-	-	-

FIG. 16B Efficacy of rat-human chimeric anti-Notch3 ADCs dosed at 5mg/kg in MDA-MB-468 breast xenografts

	MDA-MB-468 Breast xenografts, tumor volume (mm^3 ± SEM)							
Day	PBS	ch75-mc3377	ch75-me0131	ch75-MALPEG6 C2-0131	ch75-mc0131	huNeg8.8-mc0131	huNeg8.8-mc3377	huNeg8.8-me0131
-1	303 ±10	304 ±19	303 ±18	308 ±22	305 ±14	306 ±14	302 ±15	306 ±21
2	344 ±14	315 ±26	348 ±21	376 ±16	354 ±7	340 ±16	363 ±25	343 ±26
5	360 ±17	339 ±25	339 ±16	325 ±23	346 ±14	349 ±19	366 ±19	349 ±31
8	439 ±28	340 ±20	362 ±21	346 ±27	368 ±15	437 ±35	431 ±25	421 ±36
12	533 ±41	337 ±22	311 ±26	312 ±31	360 ±18	492 ±27	449 ±30	486 ±41
15	542 ±40	304 ±23	291 ±22	271 ±18	322 ±22	543 ±42	484 ±48	523 ±36
19	608 ±46	234 ±20	228 ±25	204 ±20	283 ±19	552 ±37	516 ±26	542 ±45
22	644 ±34	240 ±20	210 ±26	156 ±21	261 ±22	602 ±38	581 ±38	586 ±47
26	707 ±58	256 ±22	169 ±14	127 ±14	252 ±25	615 ±65	604 ±34	664 ±52
29	785 ±72	278 ±33	191 ±18	119 ±16	285 ±27	701 ±58	641 ±42	695 ±57
33	822 ±78	320 ±45	203 ±23	133 ±22	315 ±31	755 ±80	737 ±67	759 ±66
36	840 ±87	308 ±53	220 ±18	119 ±20	320 ±30	798 ±55	865 ±54	788 ±81
40	894 ±80	346 ±51	276 ±39	143 ±20	367 ±41	882 ±90	946 ±69	853 ±77
44	1040 ±104	373 ±49	312 ±34	162 ±29	421 ±29	1050 ±109	1055 ±54	1002 ±82
48	1174 ±146	459 ±69	362 ±58	193 ±31	455 ±42	1138 ±131	1148 ±36	1066 ±92
51	1266 ±144	539 ±83	418 ±49	237 ±31	563 ±48	1301 ±127	1368 ±57	1164 ±98
54	1244 ±166	543 ±80	422 ±45	220 ±37	592 ±52	1288 ±134	1321 ±56	1206 ±139
57	1366 ±161	607 [illegible]	474 ±65	260 ±36	665 ±56	1380 ±151	1530 ±23	1143 ±117
61	1492 ±129	659 ±100	497 ±80	275 ±36	690 ±52	1380 ±149	1607 ±39	-
64	-	718 ±117	519 ±93	363 ±45	758 ±64	1420 ±160	1580 ±47	-
68	-		636 ±117	369 ±48	-	1552 ±198	1550 ±71	-
71	-		706 ±102	377 ±65	-	-	-	-
78	-	-	906 ±137	511 ±74	-	-	-	-

FIG. 16C Efficacy of rat-human chimeric anti-Notch3 ADCs dosed at 5mg/kg in MDA-MB-468 breast xenograft

	MDA-MB-468 Breast xenografts, tumor volume (mm^3 ± SEM)														
Day	PBS	ch28-mc0131	ch28-mc3377	ch28-me0131	ch28-MALPEG6C2-0131	ch75-mc0131	ch28-vc0101	ch28-vc6780	ch75-vc0101	ch75-vc6780	huNeg8.8-mc0131	huNeg8.8-mc3377	huNeg8.8-me0131	huNeg8.8-vc0101	huNeg8.8-vc6780
-1	309 ±11	314 ±12	313 ±20	314 ±15	311 ±22	307 ±19	313 ±22	309 ±20	312 ±7	308 ±8	313 ±21	310 ±15	308 ±22	312 ±18	312 ±19
4	396 ±20	358 ±19	321 ±20	329 ±19	331 ±26	337 ±16	303 ±21	325 ±18	328 ±21	341 ±17	353 ±27	333 ±19	358 ±27	333 ±27	375 ±17
8	414 ±25	315 ±18	297 ±17	306 ±14	296 ±25	315 ±14	241 ±24	303 ±21	297 ±23	323 ±21	384 ±33	391 ±26	398 ±32	349 ±22	383 ±16
11	452 ±31	262 ±15	237 ±15	256 ±12	236 ±22	324 ±22	149 ±17	249 ±25	219 ±16	306 ±25	422 ±33	408 ±31	422 ±40	350 ±35	420 ±20
18	578 ±48	143 ±11	121 ±10	173 ±21	115 ±9	257 ±28	38 ±8	143 ±16	108 ±12	257 ±35	496 ±45	479 ±40	537 ±56	310 ±61	486 ±19
21	615 ±46	107 ±9	119 ±10	145 ±19	68 ±6	214 ±27	24 ±7	14 2±21	70 ±10	232 ±43	499 ±47	569 ±49	572 ±55	275 ±66	548 ±39
28	729 ±69	113 ±16	132 ±15	95 ±18	26 ±10	171 ±24	14 ±7	168 ±25	37 ±11	258 ±60	584 ±51	638 ±72	638 ±61	251 ±66	616 ±28
35	835 ±87	131 ±25	191 ±20	127 ±19	15 ±8	206 ±29	7 ±5	176 ±33	26 ±9	340 ±58	662 ±64	758 ±101	772 ±86	279 ±72	730 ±57
39	968 ±103	179 ±37	234 ±19	148 ±33	32 ±12	267 ±36	0 ±0	229 ±41	13 ±9	400 ±74	702 ±56	882 ±110	881 ±114	361 ±99	860 ±65
42	1004 ±112	168 ±35	256 ±22	174 ±37	32 ±13	256 ±38	0 ±0	242 ±41	10 ±8	420 ±72	753 ±75	945 ±123	926 ±115	362 ±90	888 ±49
46	1140 ±126	191 ±43	290 ±27	188 ±48	44 ±16	293 ±35	0 ±0	243 ±41	11 ±8	442 ±77	834 ±77	1016 ±148	1022 ±135	377 ±101	965 ±102
49	1211 ±92	233 ±56	333 ±33	207 ±45	37 ±17	334 ±46	0 ±0	295 ±52	7 ±7	495 ±86	896 ±90	1114 ±150	1060 ±130	439 ±115	1038 ±128
57	1402 ±112	298 ±67	447 ±37	272 ±59	72 ±28	400 ±53	0 ±0	369 ±65	13 ±13	652 ±110	1093 ±106	1356 ±139	1329 ±175	448 ±90	1275 ±143
60	-	328 ±69	513 ±42	336 ±67	69 ±28	472 ±59	0 ±0	373 ±61	25 ±16	688 ±118	1108 ±97	1296 ±158	1249 ±166	582 ±157	
63	-	320 ±70	516 ±44	354 ±67	67 ±29	498 ±58	0 ±0	415 ±76	21 ±14	709 ±114	1092 ±113	1376 ±137	1332 ±160	579 ±148	
67	-	379 ±85	536 ±49	371 ±77	85 ±37	563 ±63	0 ±0	462 ±94	21 ±15	798 ±136	1203 ±121	-	-	655 ±165	-
74	-	434 ±96	682 ±57	382 ±47	114 ±47		0 ±0	499 ±91	42 ±27	928 ±143	-	-	-		-
77	-	470 ±113	-	423 ±42	122 ±51	-	0 ±0	-	45 ±26	-	-	-	-	-	-
84	-	-	-	-	177 ±72	-	0 ±0	-	67 ±37	-	-	-	-	-	-
98	-	-	-	-	162 ±75	-	0 ±0	-	55 ±37	-	-	-	-	-	-
104	-	-	-	-	-	-	0 ±0	-	-	-	-	-	-	-	-
112	-	-	-	-	-	-	0 ±0	-	-	-	-	-	-	-	-
117	-	-	-	-	-	-	0 ±0	-	-	-	-	-	-	-	-
126	-	-	-	-	-	-	0 ±0	-	-	-	-	-	-	-	-

FIG. 16D

Efficacy of rat-human chimeric anti-Notch3 ADCs dosed at 5mg/kg in N87 gastric xenograft

	N87 Gastric xenografts, tumor volume (mm^3 ± SEM)							
Day	PBS	ch28-mc0131	ch28-vc0101	ch28-vc6780	ch75-vc0101	ch75-vc6780	huNeg8.8-vc0101	huNeg8.8-vc6780
-1	388 ±16	391 ±11	394 ±16	388 ±17	391 ±8	385 ±18	394 ±18	393 ±16
3	615 ±48	669 ±35	558 ±20	484 ±72	596 ±38	631 ±31	722 ±60	711 ±31
6	907 ±56	583 ±41	488 ±48	522 ±41	611 ±27	672 ±40	745 ±76	733 ±43
11	1335 ±67	623 ±50	313 ±26	416 ±48	437 ±29	568 ±74	858 ±112	1019 ±46
14	1260 ±85	452 ±48	208 ±21	297 ±62	275 ±18	447 ±87	771 ±124	988 ±86
18	1393 ±101	468 ±55	183 ±20	285 ±65	228 ±17	419 ±91	727 ±167	997 ±88
21	1701 ±117	528 ±61	189 ±25	314 ±80	221 ±28	462 ±121	775 ±180	1202 ±156
25	-	631 ±72	194 ±30	305 ±84	224 ±44	430 ±131	579 ±112	1151 ±119
28	-	579 ±78	173 ±26	291 ±88	230 ±56	427 ±133	570 ±133	1247 ±137
31	-	597 ±75	176 ±32	349 ±110	256 ±62	458 ±148	646 ±148	1310 ±160
35	-	671 ±89	214 ±45	380 ±121	326 ±72	490 ±177	685 ±163	1465 ±237
39	-	762 ±98	256 ±53	406 ±133	416 ±109	514 ±190	791 ±186	-
42	-	894 ±118	279 ±55	470 ±217	497 ±123	611 ±230	892 !S%&	-
46	-	873 ±115	279 ±58	493 ±158	549 ±156	603 ±225	912 ±248	-
50	-	1020 ±149	341 ±60	573 ±179	630 ±187	806 ±285	-	-
55	-	1055 ±193	374 ±83	560 ±174	715 ±207	600 ±238	-	-
62	-	1193 ±207	379 ±85	653 ±204	806 ±253	649 ±254	-	-
69	-	-	490 ±106	773 ±254	-	788 ±313	-	-
77	-	-	534 ±126	720 ±269	-	-	-	-
83	-	-	627 ±156	-	-	-	-	-
90	-	-	813 ±197	-	-	-	-	-
95	-	-	903 ±207	-	-	-	-	-
101	-	-	901 ±213	-	-	-	-	-

FIG. 16E Efficacy of rat-human chimeric anti-Notch3 ADCs dosed at 5mg/kg in N87 gastric xenografts

	N87 Gastric xenografts, tumor volume (mm^3 ± SEM)				
Day	PBS	ch28-mc0131	ch28-m(H2O)c-0131	ch75-mc0131	ch75-m(H2O)c-0131
-1	372 ±8	371 ±18	371 ±17	364 ±12	373 ±15
4	589 ±28	473 ±41	469 ±41	461 ±33	497 ±34
7	706 ±56	479 ±39	446 ±34	466 ±28	484 ±35
11	837 ±71	442 ±37	391 ±29	468 ±33	414 ±28
14	959 ±98	395 ±43	303 ±24	430 ±33	337 ±20
18	1069 ±106	328 ±36	231 ±27	424 ±41	279 ±14
21	1252 ±123	337 ±48	232 ±29	448 ±42	268 ±13
25	1230 ±112	324 ±55	230 ±38	422 ±45	271 ±11
28	1352 ±132	363 ±62	256 ±41	487 ±52	266 ±17
32	-	381 ±66	255 ±49	530 ±56	298 ±22
35	-	419 ±85	283 ±52	541 ±56	307 ±21
39	-	453 ±87	315 ±66	570 ±55	358 ±23
42	-	522 ±108	347 ±71	619 ±66	388 ±34
46	-	559 ±119	381 ±87	629 ±68	432 ±41
49	-	637 ±139	418 ±96	697 ±87	447 ±48
53	-	681 ±149	441 ±107	755 ±91	484 ±52
56	-	713 ±167	479 ±113	753 ±90	512 ±55
63	-	783 ±192	542 ±139	869 ±112	563 ±70
70	-	847 ±219	535 ±146	827 ±107	579 ±86
77	-	1081 ±273	726 ±191	1041 ±139	788 ±110
84	-	-	855 ±230	1172 ±165	872 ±131
91	-	-	722 ±194	1332 ±194	1015 ±169
98	-	-	757 ±204	-	1125 ±198

FIG. 17A

SEQ ID NO: 61 hu28 HC 1.0 L443C amino acid sequence

EVQLVESGGGLVQPGGSLRLSCAASGFTFRDYGMTWVRQAPGKGLEWVAYISSGSNYIYYAEAVKGRF
TISRDNAKNSLYLQMNSLRAEDTAVYYCARRGPFVLDAWGQGTLVTVSSASTKGPSVFPLAPSSKSTSG
GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW
YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSCSPG

SEQ ID NO: 62 hu28 HC 1.0 L443C nucleotide sequence

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTG
TGCAGCCTCTGGATTCACTTTCAGGGACTATGGAATGACCTGGGTCCGCCAGGCTCCAGGGAAGGG
GCTGGAGTGGGTGGCCTATATTAGTAGTGGTAGCAATTACATCTATTATGCAGAAGCGGTGAAGGGC
CGATTCACCATCTCCAGAGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG
AGGACACGGCTGTGTATTACTGTGCGAGACGAGGCCCGTTTGTTTTGGATGCCTGGGGCCAGGGAA
CCCTGGTCACCGTCTCCTCAGCGTCGACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCA
AGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG
ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTC
CTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTA
CATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCTTGT
GACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTC
TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG
GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAAT
GCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGT
CCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGC
CCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCC
CCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCC
CAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTC
CCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGC
AGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGA
GCCTCTCCTGCTCCCCGGGT

SEQ ID NO: 63 hu28 LC 1.0 κK183C amino acid sequence

DIQMTQSPSSLSASVGDRVTITCKASQSINRYLHWYQQKPGKAPKLLIYNANGLQTGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCLQHNTWPDTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP
REAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLS**C**ADYEKHKVYACEVTHQGLSSPVTKSFN
RGEC

SEQ ID NO: 64 hu28 LC 1.0 κK183C nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTT
GCAAAGCAAGTCAGAGTATTAACAGGTACTTACACTGGTATCAGCAGAAACCAGGGAAAGCCCCTAA
GCTCCTGATCTATAATGCAAACGGTTTGCAAACGGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCT
GGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTTTGCA
GCATAATACGTGGCCGGACACGTTTGGCGGAGGGACCAAGGTGGAGATCAAACGAACTGTGGCTG
CACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGC
CTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGG
GTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCC
TGACGCTGAGCTGCGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCC
TGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGT

FIG. 17B

SEQ ID NO: 65 hu28 HC 1.0 L443C/K392C amino acid sequence

EVQLVESGGGLVQPGGSLRLSCAASGFTFRDYGMTWVRQAPGKGLEWVAYISSGSNYIYYAEAVKGRF
TISRDNAKNSLYLQMNSLRAEDTAVYYCARRGPFVLDAWGQGTLVTVSSASTKGPSVFPLAPSSKSTSG
GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW
YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYCTTPPVLDSDGSFFLYSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSCSPG

SEQ ID NO: 66 hu28 HC 1.0 L443C/K392C nucleotide sequence

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTG
TGCAGCCTCTGGATTCACTTTCAGGGACTATGGAATGACCTGGGTCCGCCAGGCTCCAGGGAAGGG
GCTGGAGTGGGTGGCCTATATTAGTAGTGGTAGCAATTACATCTATTATGCAGAAGCGGTGAAGGGC
CGATTCACCATCTCCAGAGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG
AGGACACGGCTGTGTATTACTGTGCGAGACGAGGCCCGTTTGTTTTGGATGCCTGGGGCCAGGGAA
CCCTGGTCACCGTCTCCTCAGCGTCGACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCA
AGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG
ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTC
CTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTA
CATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCTTGT
GACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTC
TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG
GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAAT
GCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGT
CCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGC
CCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCC
CCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCC
CAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACTGCACCACGCCTC
CCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGC
AGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGA
GCCTCTCCTGCTCCCCGGGT