FIGURE 1A

Protein sequence encoding residues 2-393 of human MEK1 with deletion from residues 32-51, mutations S218E and S222D, and an N-terminal 6-histidine tag [SEQ ID NO: 1]

```
Met Ser Tyr Tyr His His His His His His Asp Tyr Asp Ile Pro Thr
1               5                  10                  15

Thr Glu Asn Leu Tyr Phe Gln Gly Ala Met Gly Ser Pro Lys Lys Lys
            20                  25                  30

Pro Thr Pro Ile Gln Leu Asn Pro Ala Pro Asp Gly Ser Ala Val Asn
        35                  40                  45

Gly Thr Ser Ser Ala Glu Thr Asn Leu Glu Ala Phe Leu Thr Gln Lys
    50                  55                  60

Gln Lys Val Gly Glu Leu Lys Asp Asp Asp Phe Glu Lys Ile Ser Glu
65                  70                  75                  80

Leu Gly Ala Gly Asn Gly Gly Val Val Phe Lys Val Ser His Lys Pro
                85                  90                  95

Ser Gly Leu Val Met Ala Arg Lys Leu Ile His Leu Glu Ile Lys Pro
            100                 105                 110

Ala Ile Arg Asn Gln Ile Ile Arg Glu Leu Gln Val Leu His Glu Cys
        115                 120                 125

Asn Ser Pro Tyr Ile Val Gly Phe Tyr Gly Ala Phe Tyr Ser Asp Gly
    130                 135                 140

Glu Ile Ser Ile Cys Met Glu His Met Asp Gly Gly Ser Leu Asp Gln
145                 150                 155                 160

Val Leu Lys Lys Ala Gly Arg Ile Pro Glu Gln Ile Leu Gly Lys Val
                165                 170                 175

Ser Ile Ala Val Ile Lys Gly Leu Thr Tyr Leu Arg Glu Lys His Lys
            180                 185                 190
```

FIGURE 1B

```
Ile Met His Arg Asp Val Lys Pro Ser Asn Ile Leu Val Asn Ser Arg
        195                 200                 205

Gly Glu Ile Lys Leu Cys Asp Phe Gly Val Ser Gly Gln Leu Ile Asp
    210                 215                 220

Glu Met Ala Asn Asp Phe Val Gly Thr Arg Ser Tyr Met Ser Pro Glu
225                 230                 235                 240

Arg Leu Gln Gly Thr His Tyr Ser Val Gln Ser Asp Ile Trp Ser Met
                245                 250                 255

Gly Leu Ser Leu Val Glu Met Ala Val Gly Arg Tyr Pro Ile Pro Pro
            260                 265                 270

Pro Asp Ala Lys Glu Leu Glu Leu Met Phe Gly Cys Gln Val Glu Gly
        275                 280                 285

Asp Ala Ala Glu Thr Pro Pro Arg Pro Arg Thr Pro Gly Arg Pro Leu
    290                 295                 300

Ser Ser Tyr Gly Met Asp Ser Arg Pro Pro Met Ala Ile Phe Glu Leu
305                 310                 315                 320

Leu Asp Tyr Ile Val Asn Glu Pro Pro Pro Lys Leu Pro Ser Gly Val
                325                 330                 335

Phe Ser Leu Glu Phe Gln Asp Phe Val Asn Lys Cys Leu Ile Lys Asn
            340                 345                 350

Pro Ala Glu Arg Ala Asp Leu Lys Gln Leu Met Val His Ala Phe Ile
        355                 360                 365

Lys Arg Ser Asp Ala Glu Glu Val Asp Phe Ala Gly Trp Leu Cys Ser
    370                 375                 380

Thr Ile Gly Leu Asn Gln Pro Ser Thr Pro Thr His Ala Ala Gly Val
385                 390                 395                 400
```

FIGURE 1C

DNA sequence encoding SEQ ID NO: 1 [SEQ ID NO: 2]

```
atgtcgtact accatcacca tcaccatcac gattacgata tcccaacgac cgaaaacctg     60
tattttcagg gcgccatggg atcccccaag aagaagccga cgcccatcca gctgaacccg    120
gcccccgacg gctctgcagt taacgggacc agctctgcgg agaccaactt ggaggccttt    180
cttacccaga agcagaaggt gggagaactg aaggatgacg actttgagaa gatcagtgag    240
ctgggggctg gcaatggcgg tgtggtgttc aaggtctccc acaagccttc tggcctggtc    300
atggccagaa agctaattca tctggagatc aaacccgcaa tccggaacca gatcataagg    360
gagctgcagg ttctgcatga gtgcaactct ccgtacatcg tgggcttcta tggtgcgttc    420
tacagcgatg gcgagatcag tatctgcatg gagcacatgg atggaggttc tctggatcaa    480
gtcctgaaga aagctggaag aattcctgaa caaattttag gaaaagttag cattgctgta    540
ataaaaggcc tgacatatct gagggagaag cacaagatca tgcacagaga tgtcaagccc    600
tccaacatcc tagtcaactc ccgtggggag atcaagctct gtgactttgg ggtcagcggg    660
cagctcatcg acgaaatggc caacgacttc gtgggcacaa ggtcctacat gtcgccagaa    720
agactccagg ggactcatta ctctgtgcag tcagacatct ggagcatggg actgtctctg    780
gtagagatgg cggttgggag gtatcccatc cctcctccag atgccaagga gctggagctg    840
atgtttgggt gccaggtgga aggagatgcg gctgagaccc cacccaggcc aaggaccccc    900
gggaggcccc ttagctcata cggaatggac agccgacctc ccatggcaat ttttgagttg    960
ttggattaca tagtcaacga gcctcctcca aaactgccca gtggagtgtt cagtctggaa   1020
tttcaagatt ttgtgaataa atgcttaata aaaaaccccg cagagagagc agatttgaag   1080
caactcatgg ttcatgcttt tatcaagaga tctgatgctg aggaagtgga ttttgcaggt   1140
tggctctgct ccaccatcgg ccttaaccag cccagcacac caacccatgc tgctggcgtc   1200
taa                                                                 1203
```

FIGURE 1D

Protein sequence encoding residues 1-400 of human MEK2 with mutations S222E and S226D, and an N-terminal 6-histidine tag [SEQ ID NO: 3]

```
Met Ser Tyr Tyr His His His His His His Asp Tyr Asp Ile Pro Thr
1               5                  10                  15

Thr Glu Asn Leu Tyr Phe Gln Gly Ala Met Glu Pro Met Leu Ala Arg
            20                  25                  30

Arg Lys Pro Val Leu Pro Ala Leu Thr Ile Asn Pro Thr Ile Ala Glu
        35                  40                  45

Gly Pro Ser Pro Thr Ser Glu Gly Ala Ser Glu Ala Asn Leu Val Asp
    50                  55                  60

Leu Gln Lys Lys Leu Glu Glu Leu Glu Leu Asp Glu Gln Gln Lys Lys
65                  70                  75                  80

Arg Leu Glu Ala Phe Leu Thr Gln Lys Ala Lys Val Gly Glu Leu Lys
                85                  90                  95

Asp Asp Asp Phe Glu Arg Ile Ser Glu Leu Gly Ala Gly Asn Gly Gly
            100                 105                 110

Val Val Thr Lys Val Gln His Arg Pro Ser Gly Leu Ile Met Ala Arg
        115                 120                 125

Lys Leu Ile His Leu Glu Ile Lys Pro Ala Ile Arg Asn Gln Ile Ile
    130                 135                 140

Arg Glu Leu Gln Val Leu His Glu Cys Asn Ser Pro Tyr Ile Val Gly
145                 150                 155                 160

Phe Tyr Gly Ala Phe Tyr Ser Asp Gly Glu Ile Ser Ile Cys Met Glu
                165                 170                 175

His Met Asp Gly Gly Ser Leu Asp Gln Val Leu Lys Glu Ala Lys Arg
            180                 185                 190
```

FIGURE 1E

```
Ile Pro Glu Glu Ile Leu Gly Lys Val Ser Ile Ala Val Leu Arg Gly
        195                 200                 205

Leu Ala Tyr Leu Arg Glu Lys His Gln Ile Met His Arg Asp Val Lys
    210                 215                 220

Pro Ser Asn Ile Leu Val Asn Ser Arg Gly Glu Ile Lys Leu Cys Asp
225                 230                 235                 240

Phe Gly Val Ser Gly Gln Leu Ile Asp Glu Met Ala Asn Asp Phe Val
                245                 250                 255

Gly Thr Arg Ser Tyr Met Ala Pro Glu Arg Leu Gln Gly Thr His Tyr
            260                 265                 270

Ser Val Gln Ser Asp Ile Trp Ser Met Gly Leu Ser Leu Val Glu Leu
        275                 280                 285

Ala Val Gly Arg Tyr Pro Ile Pro Pro Pro Asp Ala Lys Glu Leu Glu
    290                 295                 300

Ala Ile Phe Gly Arg Pro Val Val Asp Gly Glu Glu Gly Glu Pro His
305                 310                 315                 320

Ser Ile Ser Pro Arg Pro Arg Pro Pro Gly Arg Pro Val Ser Gly His
                325                 330                 335

Gly Met Asp Ser Arg Pro Ala Met Ala Ile Phe Glu Leu Leu Asp Tyr
            340                 345                 350

Ile Val Asn Glu Pro Pro Pro Lys Leu Pro Asn Gly Val Phe Thr Pro
        355                 360                 365

Asp Phe Gln Glu Phe Val Asn Lys Cys Leu Ile Lys Asn Pro Ala Glu
    370                 375                 380

Arg Ala Asp Leu Lys Met Leu Thr Asn His Thr Phe Ile Lys Arg Ser
385                 390                 395                 400
```

FIGURE 1F

```
Glu Val Glu Glu Val Asp Phe Ala Gly Trp Leu Cys Lys Thr Leu Arg
                405                 410                 415

Leu Asn Gln Pro Gly Thr Pro Thr Arg Thr Ala Val
            420                 425
```

DNA sequence encoding SEQ ID NO: 3 [SEQ ID NO: 4]

```
atgtcgtact accatcacca tcaccatcac gattacgata tcccaacgac cgaaaacctg     60
tattttcagg gcgccatgga acccatgctg gcccggagga agccggtgct gccggcgctc    120
accatcaacc ctaccatcgc cgagggccca tcccctacca gcgagggcgc ctccgaggca    180
aacctggtgg acctgcagaa gaagctggag gagctggaac ttgacgagca gcagaagaag    240
cggctggaag cctttctcac ccagaaagcc aaggtcggcg aactcaaaga cgatgacttc    300
gaaaggatct cagagctggg cgcgggcaac ggcggggtgg tcaccaaagt ccagcacaga    360
ccctcgggcc tcatcatggc caggaagctg atccaccttg agatcaagcc ggccatccgg    420
aaccagatca tccgcgagct gcaggtcctg cacgaatgca actcgccgta catcgtgggc    480
ttctacgggg ccttctacag tgacggggag atcagcattt gcatggaaca catggacggc    540
ggctccctgg accaggtgct gaaagaggcc aagaggattc ccgaggagat cctggggaaa    600
gtcagcatcg cggttctccg gggcttggcg tacctccgag agaagcacca gatcatgcac    660
cgagatgtga agccctccaa catcctcgtg aactctagag gggagatcaa gctgtgtgac    720
ttcggggtga gcggccagct catagacgaa atggccaacg acttcgtggg cacgcgctcc    780
tacatggctc cggagcggtt gcagggcaca cattactcgg tgcagtcgga catctggagc    840
atgggcctgt ccctggtgga gctggccgtc ggaaggtacc ccatcccccc gcccgacgcc    900
aaagagctgg aggccatctt tggccggccc gtggtcgacg gggaagaagg agagcctcac    960
agcatctcgc ctcggccgag gccccccggg cgccccgtca gcggtcacgg gatggatagc   1020
cggcctgcca tggccatctt tgaactcctg gactatattg tgaacgagcc acctcctaag   1080
```

FIGURE 1G

```
ctgcccaacg gtgtgttcac ccccgacttc caggagtttg tcaataaatg cctcatcaag   1140

aacccagcgg agcgggcgga cctgaagatg ctcacaaacc acaccttcat caagcggtcc   1200

gaggtggaag aagtggattt tgccggctgg ttgtgtaaaa ccctgcggct gaaccagccc   1260

ggcacaccca cgcgcaccgc cgtgtaa                                       1287
```

Protein sequence encoding residues 1-379 of human ERK1 with an N-terminal GST tag [SEQ ID NO: 5]

```
Met Ser Pro Ile Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro
1               5                  10                  15

Thr Arg Leu Leu Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu
            20                  25                  30

Tyr Glu Arg Asp Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu
        35                  40                  45

Gly Leu Glu Phe Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys
    50                  55                  60

Leu Thr Gln Ser Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn
65                  70                  75                  80

Met Leu Gly Gly Cys Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu
                85                  90                  95

Gly Ala Val Leu Asp Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser
            100                 105                 110

Lys Asp Phe Glu Thr Leu Lys Val Asp Phe Leu Ser Lys Leu Pro Glu
        115                 120                 125

Met Leu Lys Met Phe Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn
    130                 135                 140

Gly Asp His Val Thr His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp
145                 150                 155                 160
```

FIGURE 1H

```
Val Val Leu Tyr Met Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu
                165                 170                 175

Val Cys Phe Lys Lys Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr
            180                 185                 190

Leu Lys Ser Ser Lys Tyr Ile Ala Trp Pro Leu Gln Gly Trp Gln Ala
        195                 200                 205

Thr Phe Gly Gly Gly Asp His Pro Pro Lys Ser Asp Leu Glu Val Leu
    210                 215                 220

Phe Gln Gly Pro Leu Gly Ser Pro Asn Ser Gly Met Ala Ala Ala Ala
225                 230                 235                 240

Ala Gln Gly Gly Gly Gly Gly Glu Pro Arg Arg Thr Glu Gly Val Gly
                245                 250                 255

Pro Gly Val Pro Gly Glu Val Glu Met Val Lys Gly Gln Pro Phe Asp
            260                 265                 270

Val Gly Pro Arg Tyr Thr Gln Leu Gln Tyr Ile Gly Glu Gly Ala Tyr
        275                 280                 285

Gly Met Val Ser Ser Ala Tyr Asp His Val Arg Lys Thr Arg Val Ala
    290                 295                 300

Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln Arg Thr
305                 310                 315                 320

Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe Arg His Glu Asn Val Ile
                325                 330                 335

Gly Ile Arg Asp Ile Leu Arg Ala Ser Thr Leu Glu Ala Met Arg Asp
            340                 345                 350

Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys Leu Leu
        355                 360                 365
```

FIGURE 1I

```
Lys Ser Gln Gln Leu Ser Asn Asp His Ile Cys Tyr Phe Leu Tyr Gln
    370                 375                 380

Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu His Arg
385                 390                 395                 400

Asp Leu Lys Pro Ser Asn Leu Leu Ile Asn Thr Thr Cys Asp Leu Lys
                405                 410                 415

Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala Asp Pro Glu His Asp His
            420                 425                 430

Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg Ala Pro
        435                 440                 445

Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp Ile Trp
    450                 455                 460

Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro Ile Phe
465                 470                 475                 480

Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly Ile Leu
                485                 490                 495

Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile Asn Met Lys Ala
            500                 505                 510

Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys Thr Lys Val Ala Trp Ala
        515                 520                 525

Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala Leu Asp Leu Leu Asp Arg
    530                 535                 540

Met Leu Thr Phe Asn Pro Asn Lys Arg Ile Thr Val Glu Glu Ala Leu
545                 550                 555                 560

Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Thr Asp Glu Pro Val
                565                 570                 575
```

FIGURE 1J

```
Ala Glu Glu Pro Phe Thr Phe Ala Met Glu Leu Asp Asp Leu Pro Lys
            580                 585                 590

Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu Thr Ala Arg Phe Gln Pro
        595                 600                 605

Gly Val Leu Glu Ala Pro
    610
```

DNA sequence encoding SEQ ID NO: 5 [SEQ ID NO: 6]

```
atgtccccta tactaggtta ttggaaaatt aagggccttg tgcaacccac tcgacttctt     60
ttggaatatc ttgaagaaaa atatgaagag catttgtatg agcgcgatga aggtgataaa    120
tggcgaaaca aaaagtttga attgggtttg gagtttccca atcttcctta ttatattgat    180
ggtgatgtta aattaacaca gtctatggcc atcatacgtt atatagctga caagcacaac    240
atgttgggtg gttgtccaaa agagcgtgca gagatttcaa tgcttgaagg agcggttttg    300
gatattagat acggtgtttc gagaattgca tatagtaaag actttgaaac tctcaaagtt    360
gattttctta gcaagctacc tgaaatgctg aaaatgttcg aagatcgttt atgtcataaa    420
acatatttaa atggtgatca tgtaacccat cctgacttca tgttgtatga cgctcttgat    480
gttgttttat acatggaccc aatgtgcctg gatgcgttcc caaaattagt ttgttttaaa    540
aaacgtattg aagctatccc acaaattgat aagtacttga aatccagcaa gtatatagca    600
tggcctttgc agggctggca agccacgttt ggtggtggcg accatcctcc aaaatcggat    660
ctggaagttc tgttccaggg gcccctggga tccccgaatt ccgggatggc ggcggcggcg    720
gctcaggggg gcgggggcgg ggagccccgt agaaccgagg gggtcggccc gggggtcccg    780
ggggaggtgg agatggtgaa ggggcagccg ttcgacgtgg gcccgcgcta cacgcagttg    840
cagtacatcg gcgagggcgc gtacggcatg gtcagctcgg cctatgacca cgtgcgcaag    900
actcgcgtgg ccatcaagaa gatcagcccc ttcgaacatc agacctactg ccagcgcacg    960
ctccgggaga tccagatcct gctgcgcttc cgccatgaga atgtcatcgg catccgagac   1020
attctgcggg cgtccaccct ggaagccatg agagatgtct acattgtgca ggacctgatg   1080
```

FIGURE 1K

gagactgacc tgtacaagtt gctgaaaagc cagcagctga gcaatgacca tatctgctac 1140

ttcctctacc agatcctgcg gggcctcaag tacatccact ccgccaacgt gctccaccga 1200

gatctaaagc cctccaacct gctcatcaac accacctgcg accttaagat ttgtgatttc 1260

ggcctggccc ggattgccga tcctgagcat gaccacaccg gcttcctgac ggagtatgtg 1320

gctacgcgct ggtaccgggc cccagagatc atgctgaact ccaagggcta taccaagtcc 1380

atcgacatct ggtctgtggg ctgcattctg gctgagatgc tctctaaccg gcccatcttc 1440

cctggcaagc actacctgga tcagctcaac cacattctgg gcatcctggg ctccccatcc 1500

caggaggacc tgaattgtat catcaacatg aaggcccgaa actacctaca gtctctgccc 1560

tccaagacca aggtggcttg ggccaagctt ttccccaagt cagactccaa agcccttgac 1620

ctgctggacc ggatgttaac ctttaacccc aataaacgga tcacagtgga ggaagcgctg 1680

gctcacccct acctggagca gtactatgac ccgacggatg agccagtggc cgaggagccc 1740

ttcaccttcg ccatggagct ggatgaccta cctaaggagc ggctgaagga gctcatcttc 1800

caggagacag cacgcttcca gcccggagtg ctggaggccc cctag 1845