Figure 1: Identification of the differentially expressed gene PRKX by GeneChip microarray analysis

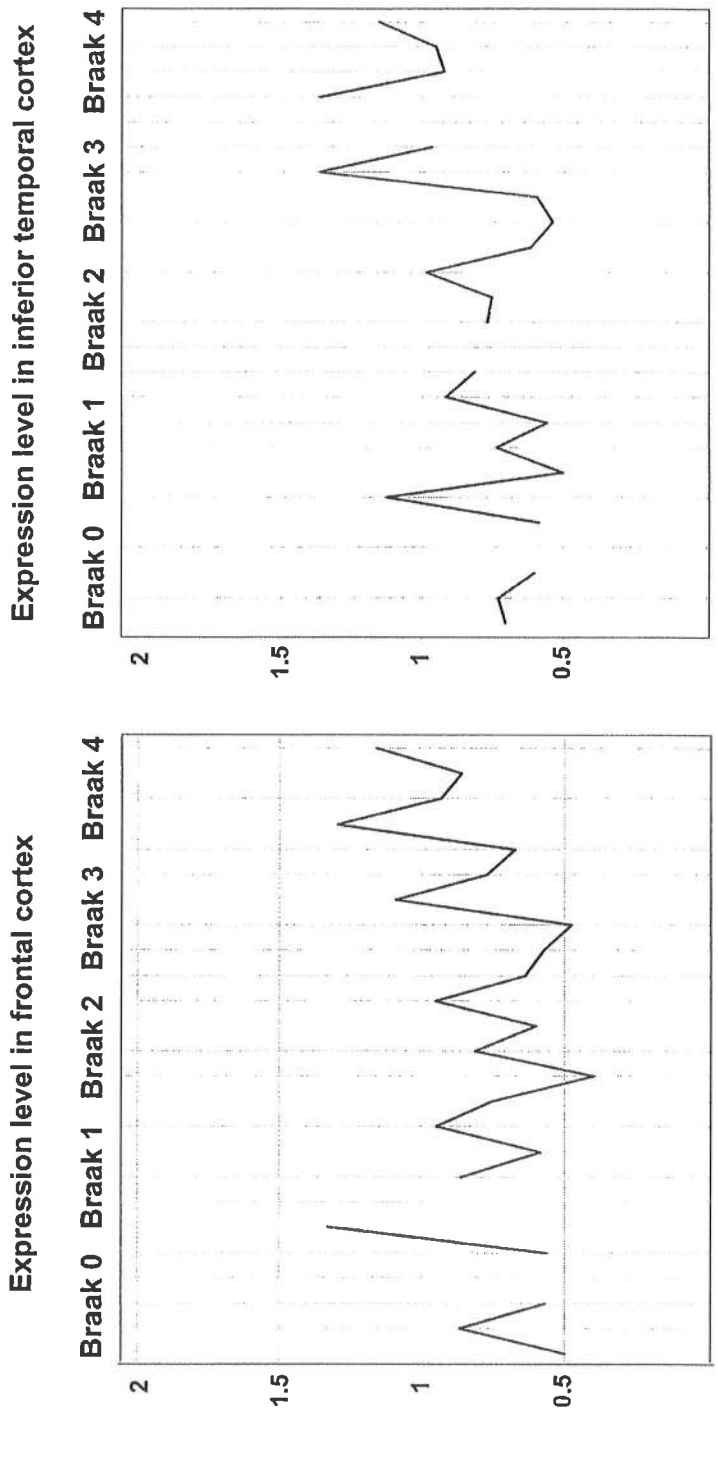


Figure 2: Analysis of PRKX mRNA expression by quantitative PCR

measured data of PRKX mRNA expression in frontal and inferior temporal cortices in Braak stages 0 – 4

Donor	Braak stage	Frontal	Temporal
C011	0	88.8333	67.4087
C012	0	110.8079	94.9113
C026	0	53.9243	46.2760
C027	0	47.5921	51.7613
C032	0	76.9483	71.6816
C014	1	212.5791	185.3968
C028	1	46.8136	56.5168
C029	1	86.6158	126.5573
C030	1	#DIV/0!	#DIV/0!
C036	1	#DIV/0!	#DIV/0!
C038	1	88.8687	101.0214
C039	1	52.7322	31.7496
C008	2	35.5761	37.1341
C031	2	13.7663	12.6466
C033	2	79.7729	61.8957
C034	2	72.2403	57.8616
DE03	2	46.1562	36.7279
C025	3	42.1552	41.9959
DE07	3	110.3829	156.0494
DE11	3	74.2368	84.1129
C057	3	103.9013	100.0807
P012	4	163.0308	210.3438
P046	4	142.0928	169.0411
P047	4	73.6209	102.7507
P068	4	117.7727	115.7678

Figure 3: Statistical analysis of differential PRKX mRNA expression

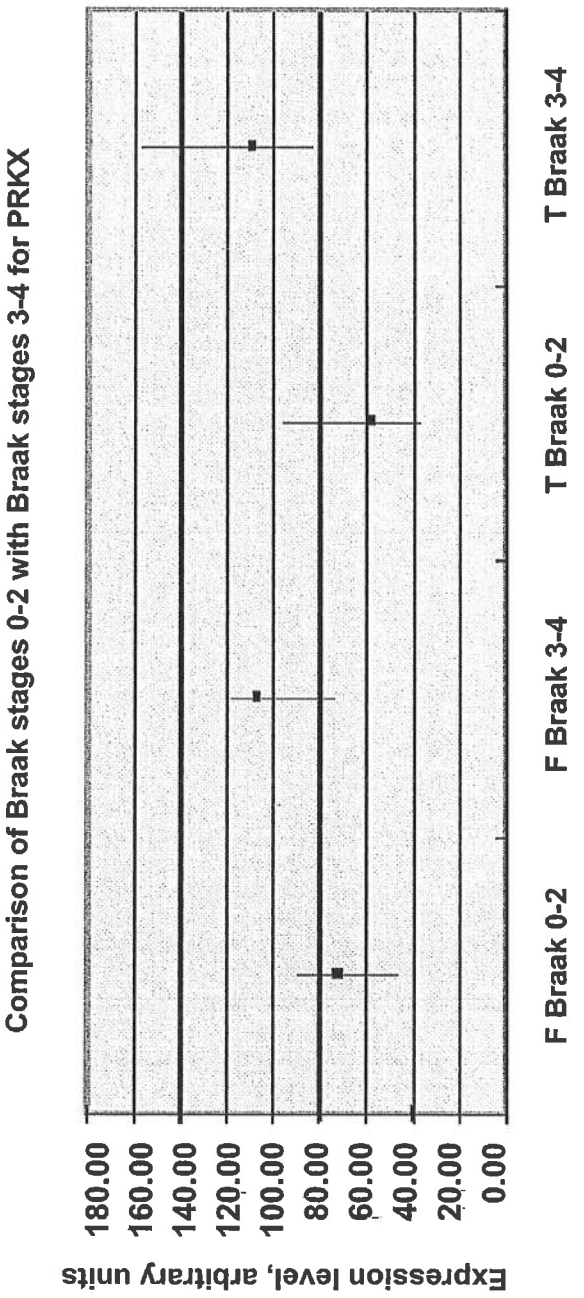


Figure 4 : A) SEQ ID NO: 1, amino acid sequence of human PRKX protein

Length: 358 aa

```
  1  MEAPGLAQAA AAESDSRKVA EETPDGAPAL CPSPEALSPE PPVYSLQDFD
 51  TLATVGTGTF GRVHLVKEKT AKHFFALKVM SIPDVIRLKQ EQHVHNEKSV
101  LKEVSHPFLI RLFWTWHDER FLYMLMEYVP GGELFSYLRN RGRFSSTTGL
151  FYSAEIICAI EYLHSKEIVY RDLKPENILL DRDGHIKLTD FGFAKKLVDR
201  TWTLCGTPEY LAPEVIQSKG HGRAVDWWAL GILIFEMLSG FPPFFDDNPF
251  GIYQKILAGK IDFPRHLDFH VKDLIKKLLV VDRTRRLGNM KNGANDVKHH
301  RWFRSVDWEA VPQRKLKPPI VPKIAGDGDT SNFETYPEND WDTAAPVPQK
351  DLEIFKNF
```

Figure 4 : B) SEQ ID NO: 2, amino acid sequence of human PRKY protein

Length: 277 aa

```
  1  MEAPGPAQAA AAESNSREVT EDAADWAPAL CPSPEARSPE APAYRLQDCD
 51  ALVTMGTGTF GRVHLVKEKT AKHFFALKVM SIPDVIRRKQ EQHVHNEKSV
101  LKEVSHPFLI RLFWTWHEER FLYMLMEYVP GGELFSYLRN RGHFSSTTGL
151  FYSAEIICAI EYLHSKEIVY RDLKPENILL DRDGHIKLTD FGFAKKLVDR
201  TWTLCGTPEY LAPEVIQSKG HGRAVDWWAL GILIFEMLSG FPPFFDDNPF
251  GIYQKILAGK LYFPRHLDFH VKTGRMM
```

Figure 5 : A) SEQ ID NO: 3, nucleotide sequence of human PRKX cDNA

Length: 2350 bp

```
   1  GCCGCCCAGC CATTGTCCCC GTCGCTCCGT CAGCCGCGCC GGACCGCGCA
  51  CCAGGAGGCG AGAGCGCGCA TGGGGAGCCT CTGTTGATGC CGCCGCCGCG
 101  CCGCCCTCCG AGGCTGCGTC CCGGGAAGCC CGGCTCCCCG AGCGCTCCGG
 151  CCTGGCCCGG TGCCCCGGAC CTGAGTGCGT CCCCATGGAG GCGCCCGGGC
 201  TGGCCCAGGC GGCCGCGGCG GAGAGCGACT CCCGCAAGGT GGCGGAGGAG
 251  ACCCCCGACG GGGCGCCCGC GCTCTGCCCC AGCCCTGAGG CGCTGTCGCC
 301  GGAGCCGCCT GTGTACAGCC TGCAGGACTT TGACACGCTG GCCACCGTGG
 351  GCACTGGGAC GTTCGGGCGG GTGCACCTGG TGAAGGAGAA GACAGCCAAG
 401  CATTTCTTCG CCCTCAAGGT GATGAGCATT CCTGACGTCA TCCGCCTAAA
 451  GCAGGAGCAA CACGTACACA ATGAGAAGTC TGTCCTGAAG GAAGTCAGCC
 501  ACCCGTTCCT CATCAGGCTG TTCTGGACGT GGCATGACGA GCGCTTCCTC
 551  TACATGCTCA TGGAGTACGT GCCGGGCGGC GAGCTCTTCA GCTACCTGCG
 601  CAACCGGGGG CGCTTCTCCA GCACCACGGG GCTCTTCTAC TCTGCAGAGA
 651  TCATCTGTGC CATCGAGTAC CTGCACTCCA AAGAGATCGT CTACAGGGAC
 701  TTGAAGCCAG AGAACATCCT GCTGGATAGG GATGGCCACA TTAAGCTCAC
 751  GGACTTTGGG TTCGCCAAGA AGCTGGTAGA CAGGACTTGG ACCCTCTGTG
 801  GAACACCCGA GTACCTAGCC CCCGAAGTCA TTCAGAGCAA GGGCCACGGA
 851  AGGGCCGTGG ACTGGTGGGC CCTCGGCATC CTGATATTCG AGATGCTTTC
 901  GGGGTTTCCT CCGTTTTTTG ATGACAACCC GTTTGGCATT TATCAGAAAA
 951  TTCTTGCAGG CAAAATAGAT TTCCCCAGAC ATTTGGATTT CCATGTAAAA
1001  GACCTCATTA AGAAACTGCT CGTGGTTGAC AGAACAAGGC GATTAGGAAA
1051  CATGAAGAAC GGGGCGAATG ATGTGAAGCA TCATCGGTGG TTCCGCTCCG
1101  TGGACTGGGA AGCTGTTCCG CAGAGAAAAC TGAAGCCTCC CATCGTGCCC
1151  AAGATAGCTG GTGACGGCGA CACTTCCAAC TTCGAAACTT ACCCTGAGAA
1201  TGACTGGGAC ACAGCCGCGC CCGTGCCGCA GAAGGATTTA GAAATCTTCA
1251  AGAATTTCTG AGGACAGGAG CTCACATCTG GAAGAAACAG GAAGATTGGA
1301  ATCTGCCTGG AACAAAGAAC TGCACCTAAG CAGACCAGAA GCAAAATGTC
1351  TTCTTCACGG CATAAGGACA TCTCCACTTT TCTCTGTACC TGTGTGTATA
1401  GAAATAGATT AGAGCACAGT TGAAATTCAT GGAACTGGCA TTATTTAAGC
1451  AACTGGAATT CCACACTGTA GGAAGGTTTT GAAAATTGTT TGGTTGTAGA
1501  TTTTATCTTA TCCTTTAGTG TTGTGTTCCT ACTGTGATGT CTTGGTTTTT
1551  GTCATAGACT TAAGTTTATA AGTTTGAACT GGACTTGTTC GATTATAACC
1601  ACAAATTGTG TGTGTGTGTG TGTGTGTGTG TGTGTGTGTG TGTGTGTGTG
1651  TGTATGCCTG TGTGTATATA TAGAAGTCAT TATGGCAGAT GCACAGAAAT
1701  TGTGCAGTGA TGTAAATGTT CATACTTTAC AGAGCCTATA ATTTTTATTT
1751  TTCAATTTGT TTTTTCAAAA ATCTCTTCTC GGGGACAACA TCTGAAGGGT
1801  ATGTTGCATG CATTAAAAAA AATCATCTCA CATGCATTTT ATAGTTTTGG
1851  GGAAGAAAAT ATCATGGGGA GGTCTACCTT CAGTATCTTT AGTGCTTCTT
1901  ACCTGGTAAC TTGAGACTTT AAAAGAAGAA ACAAAGAGGG GAAGATATGG
1951  GAGCGAATTT ATTCCAAGAA TCTACAATGA CATTGAAGTT GTTGGAGGAA
2001  TGTACTGTAT TTAAAAAAAC CTTCTGTGAC ACATTCAAAA ATTTCATCTG
2051  AGCTGGATGC AGTGGCTTGT TCCTATAGTC CCAGCACTTT GGGAGGCTGA
2101  GGTGGGTGGA TTGCTTGAGC CCAGGAGTTG GAGACCAGTC TGGGAAACGT
2151  GGTGAGACCT CATCTCTACA AAATACAAAA AAATTAGCCG GGCATGGTGG
2201  CACGTGAGTG TAGTCTCAGC TACTCAGGAG GCTGAGATGA GAGGATCACT
2251  TGAGCCTGGG GAGGTCCAGG CCGCAGTGAT CCGAGATCAC ACCACTGCAT
2301  TCCAGCCTGG GTGACAGAGT GAGACCCTGT CCAAAAAAAA AAAAAAAAAA
```

Figure 5 : B) SEQ ID NO: 4, nucleotide sequence of human PRKY cDNA

Length: 895 bp

```
   1  GGACCTGAGT GCCTCCCCAT GGAGGCGCCC GGGCCGGCCC AGGCGGCCGC
  51  GGCGGAGAGC AACTCCCGAG AGGTGACGGA GGATGCCGCC GACTGGGCGC
 101  CCGCGCTCTG CCCCAGCCCC GAGGCGCGGT CGCCGGAGGC GCCTGCCTAC
 151  CGCCTGCAGG ACTGCGACGC GCTGGTCACC ATGGGCACTG GGACGTTCGG
 201  GCGGGTGCAC CTGGTGAAGG AGAAGACAGC CAAGCATTTC TTCGCCCTCA
 251  AGGTGATGAG CATTCCCGAC GTCATCCGCC GGAAGCAGGA GCAGCACGTG
 301  CACAATGAGA AGTCTGTCCT GAAGGAAGTC AGCCACCCGT TCCTCATCAG
 351  GCTGTTCTGG ACGTGGCATG AGGAGCGCTT CCTCTACATG CTCATGGAGT
 401  ATGTGCCGGG TGGCGAGCTC TTCAGCTACC TGCGCAACCG GGGGCACTTC
 451  TCCAGCACCA CGGGGCTCTT CTACTCTGCG GAGATCATCT GTGCCATTGA
 501  GTACCTGCAC TCCAAGGAGA TCGTCTACAG GGATTTGAAG CCGGAGAACA
 551  TCCTGCTGGA TAGGGATGGT CACATCAAGC TCACGGACTT TGGGTTTGCC
 601  AAGAAGCTGG TAGACAGGAC TTGGACCCTC TGTGGAACAC CCGAGTACCT
 651  AGCCCCCGAA GTCATTCAGA GCAAGGGCCA CGGAAGGGCC GTGGACTGGT
 701  GGGCCCTCGG CATCCTGATA TTCGAGATGC TTTCGGGGTT TCCTCCATTT
 751  TTTGATGACA ACCCGTTTGG CATTTATCAG AAAATTCTTG CAGGCAAACT
 801  ATATTTCCCC AGACATTTGG ATTTCCATGT AAAAACGGGG CGAATGATGT
 851  GAAACACCAT CGGTGGTTCC GCTCCGTGGA CTGGAAAGCT GTTCC
```

Figure 6 : A) SEQ ID NO: 5, coding nucleotide sequence of human PRKX cDNA

Length: 1077 bp

```
   1  ATGGAGGCGC CCGGGCTGGC CCAGGCGGCC GCGGCGGAGA GCGACTCCCG
  51  CAAGGTGGCG GAGGAGACCC CCGACGGGGC GCCCGCGCTC TGCCCCAGCC
 101  CTGAGGCGCT GTCGCCGGAG CCGCCTGTGT ACAGCCTGCA GGACTTTGAC
 151  ACGCTGGCCA CCGTGGGCAC TGGGACGTTC GGGCGGGTGC ACCTGGTGAA
 201  GGAGAAGACA GCCAAGCATT TCTTCGCCCT CAAGGTGATG AGCATTCCTG
 251  ACGTCATCCG CCTAAAGCAG GAGCAACACG TACACAATGA GAAGTCTGTC
 301  CTGAAGGAAG TCAGCCACCC GTTCCTCATC AGGCTGTTCT GGACGTGGCA
 351  TGACGAGCGC TTCCTCTACA TGCTCATGGA GTACGTGCCG GGCGGCGAGC
 401  TCTTCAGCTA CCTGCGCAAC CGGGGGCGCT TCTCCAGCAC CACGGGGCTC
 451  TTCTACTCTG CAGAGATCAT CTGTGCCATC GAGTACCTGC ACTCCAAAGA
 501  GATCGTCTAC AGGGACTTGA AGCCAGAGAA CATCCTGCTG GATAGGGATG
 551  GCCACATTAA GCTCACGGAC TTTGGGTTCG CCAAGAAGCT GGTAGACAGG
 601  ACTTGGACCC TCTGTGGAAC ACCCGAGTAC CTAGCCCCCG AAGTCATTCA
 651  GAGCAAGGGC CACGGAAGGG CCGTGGACTG GTGGGCCCTC GGCATCCTGA
 701  TATTCGAGAT GCTTTCGGGG TTTCCTCCGT TTTTTGATGA CAACCCGTTT
 751  GGCATTTATC AGAAAATTCT TGCAGGCAAA ATAGATTTCC CCAGACATTT
 801  GGATTTCCAT GTAAAAGACC TCATTAAGAA ACTGCTCGTG GTTGACAGAA
 851  CAAGGCGATT AGGAAACATG AAGAACGGGG CGAATGATGT GAAGCATCAT
 901  CGGTGGTTCC GCTCCGTGGA CTGGGAAGCT GTTCCGCAGA GAAAACTGAA
 951  GCCTCCCATC GTGCCCAAGA TAGCTGGTGA CGGCGACACT TCCAACTTCG
1001  AAACTTACCC TGAGAATGAC TGGGACACAG CCGCGCCCGT GCCGCAGAAG
1051  GATTTAGAAA TCTTCAAGAA TTTCTGA
```

Figure 6 : B) SEQ ID NO: 6, coding nucleotide sequence of human PRKY cDNA

Length: 834 bp

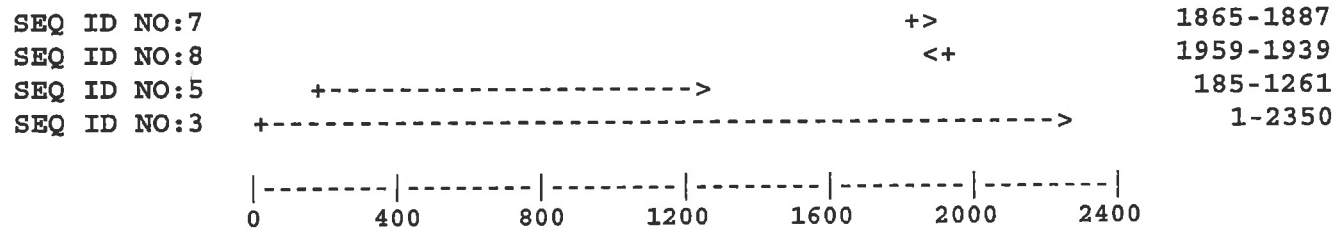
```
  1  ATGGAGGCGC CCGGGCCGGC CCAGGCGGCC GCGGCGGAGA GCAACTCCCG
 51  AGAGGTGACG GAGGATGCCG CCGACTGGGC GCCCGCGCTC TGCCCCAGCC
101  CCGAGGCGCG GTCGCCGGAG GCGCCTGCCT ACCGCCTGCA GGACTGCGAC
151  GCGCTGGTCA CCATGGGCAC TGGGACGTTC GGGCGGGTGC ACCTGGTGAA
201  GGAGAAGACA GCCAAGCATT TCTTCGCCCT CAAGGTGATG AGCATTCCCG
251  ACGTCATCCG CCGGAAGCAG GAGCAGCACG TGCACAATGA GAAGTCTGTC
301  CTGAAGGAAG TCAGCCACCC GTTCCTCATC AGGCTGTTCT GGACGTGGCA
351  TGAGGAGCGC TTCCTCTACA TGCTCATGGA GTATGTGCCG GGTGGCGAGC
401  TCTTCAGCTA CCTGCGCAAC CGGGGGCACT TCTCCAGCAC CACGGGGCTC
451  TTCTACTCTG CGGAGATCAT CTGTGCCATT GAGTACCTGC ACTCCAAGGA
501  GATCGTCTAC AGGGATTTGA AGCCGGAGAA CATCCTGCTG GATAGGGATG
551  GTCACATCAA GCTCACGGAC TTTGGGTTTG CCAAGAAGCT GGTAGACAGG
601  ACTTGGACCC TCTGTGGAAC ACCCGAGTAC CTAGCCCCCG AAGTCATTCA
651  GAGCAAGGGC CACGGAAGGG CCGTGGACTG GTGGGCCCTC GGCATCCTGA
701  TATTCGAGAT GCTTTCGGGG TTTCCTCCAT TTTTTGATGA CAACCCGTTT
751  GGCATTTATC AGAAAATTCT TGCAGGCAAA CTATATTTCC CCAGACATTT
801  GGATTTCCAT GTAAAAACGG GGCGAATGAT GTGA
```

Figure 7: Alignment of PRKX RT-PCR primers SEQ ID NO: 7 and SEQ ID NO: 8 with human PRKX cDNA, SEQ ID NO: 3

```
SEQ ID NO:7 (PRIMER A)     1 TGGGGAGGTCTACCTTCAGTATC 1
                               |||||||||||||||||||||
SEQ ID NO:3             1865 TGGGGAGGTCTACCTTCAGTATC 1887


SEQ ID NO:8 (PRIMER B)    21 GGGAAGATATGGGAGCGAATT 1
                               ||||||||||||||||||||
SEQ ID NO:3             1939 GGGAAGATATGGGAGCGAATT 1959
```

Figure 8: Schematic alignment of SEQ ID NO: 3, SEQ ID NO: 5, and RT-PCR primer sequences of PRKX



Legend:
+ 5'-end of sequence
> 3'-end of sequence
--- sequence identical to PRKX mRNA

Figure 9:
Co-deposition of PRKX protein with amyloid plaques is detected in the cerebral cortex of AD patients, but is absent from controls

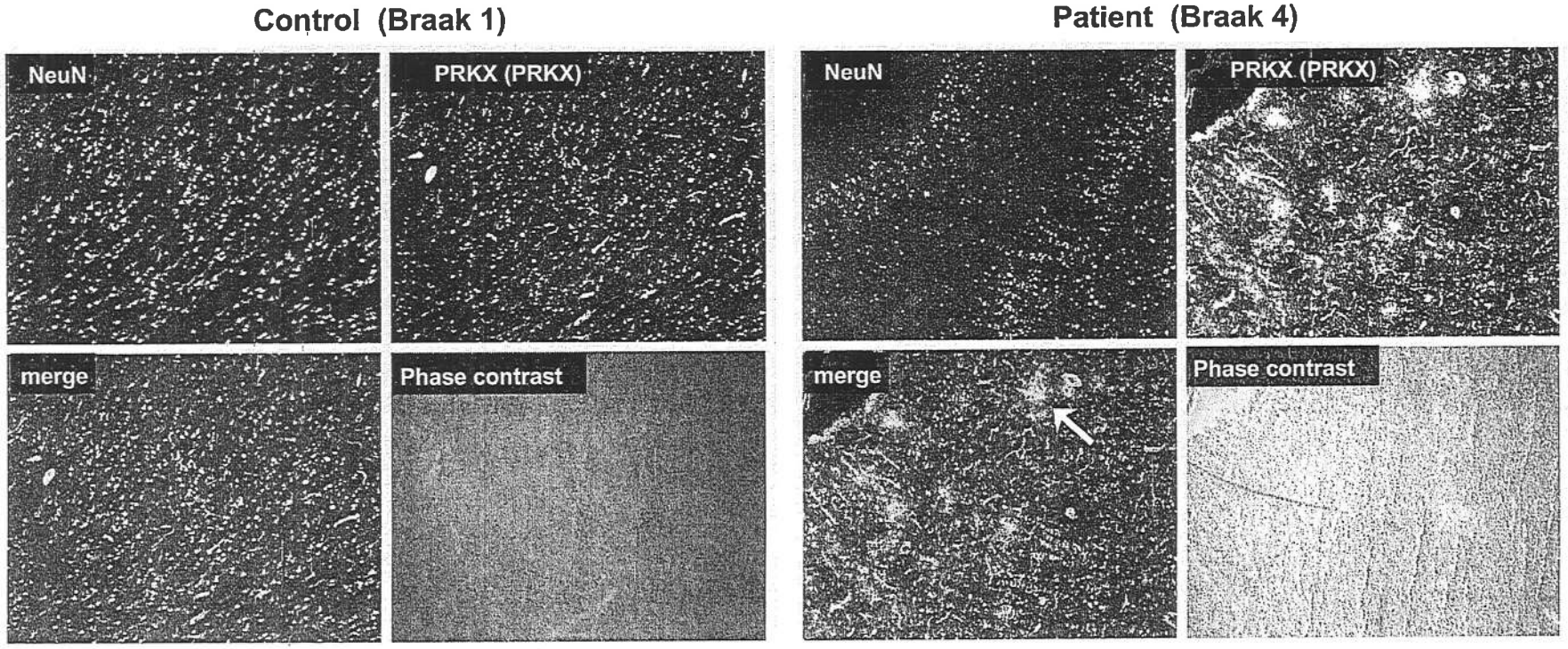


Figure 10:
Expression by astrocytes of PRKX protein is strongly enhanced in the cerebral cortex of AD patients as compared to controls

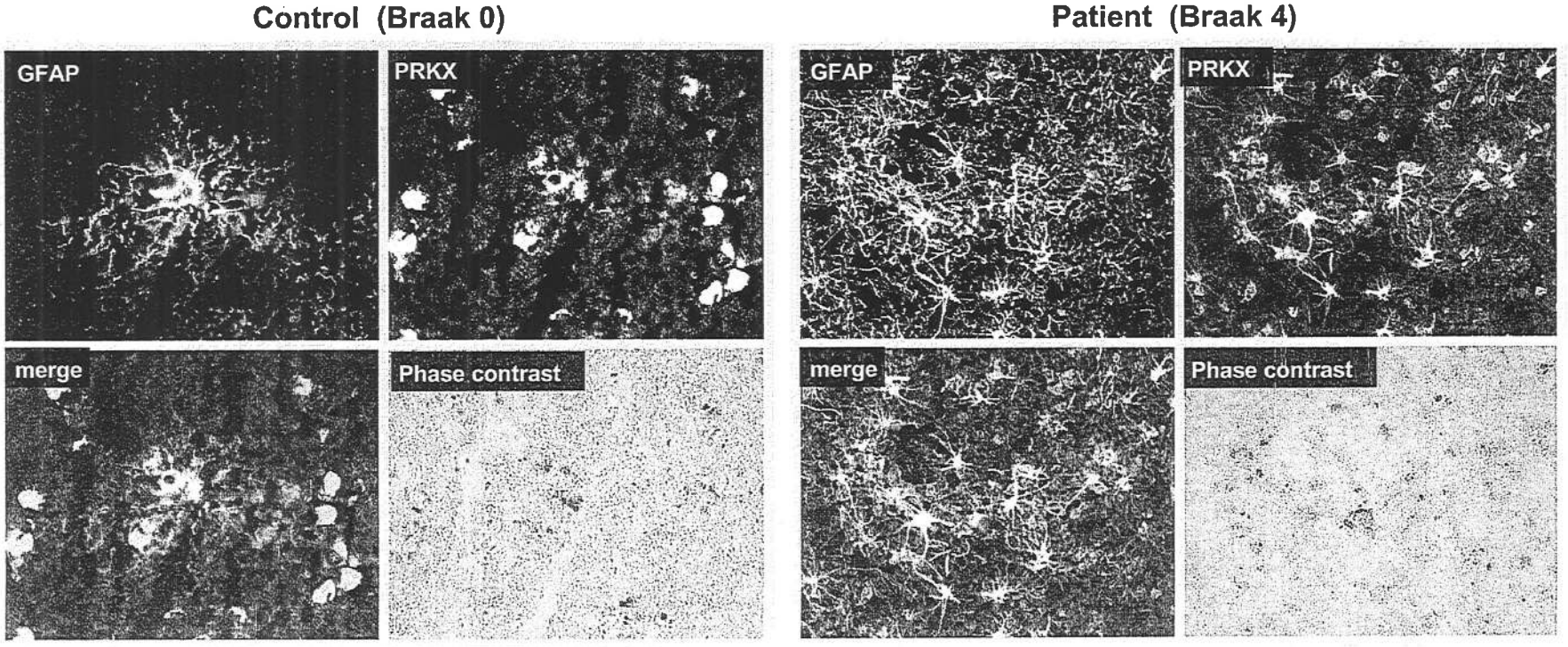


Figure 11:
PRKX protein expression is associated with plaque-associated microglial and astrocytic inflammation, which is absent from controls

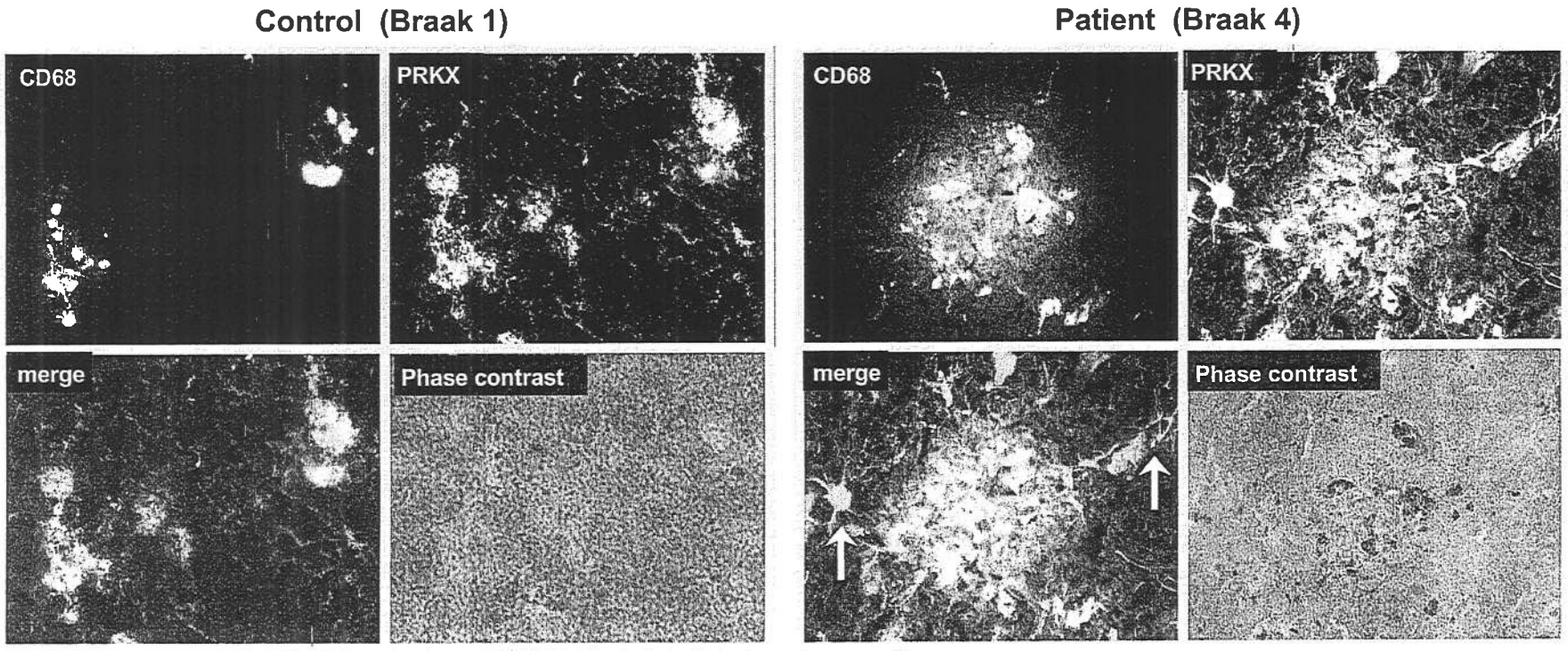
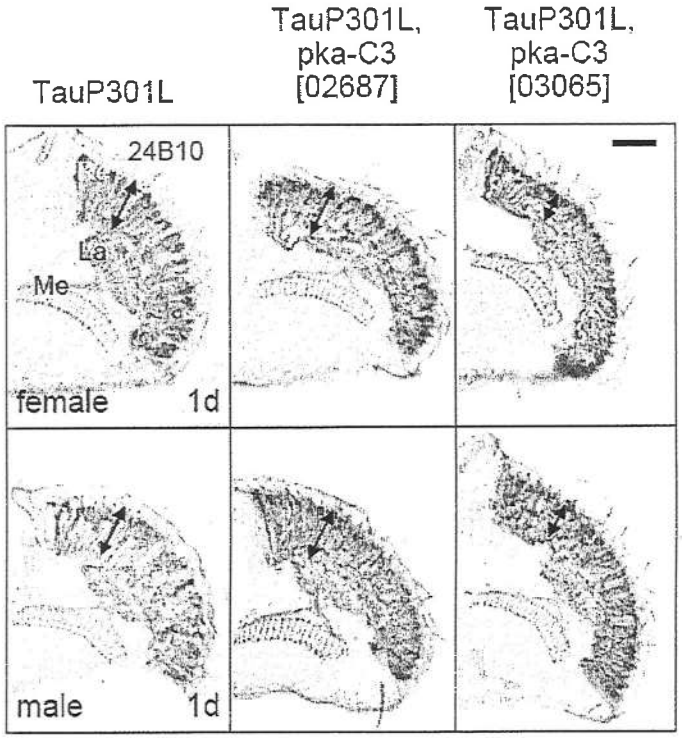


Figure 12:
LightCycler analysis of pka-C3 expression of flies expressing pka-C3 (02687) and pka-C3 (03065) under the control of GMR-Gal4 in the adult complex eye

name	**pka-C3** cycle number	pka-C3 mean	pka-C3 stdv	**rp49** cycle number	rp49 mean	rp49 stdv	rp49 factor	mean pka-C3 x factor rp49	difference	expression normalized to housekeeping gene (rp49) and efficiency (E) of **pka-C3** primer
GMR-GAL4	26,22	26,360	0,1212	20	20,087	0,0757	1,000	26,36	0,000	1,000
GMR-GAL4	26,43			20,12						
GMR-GAL4	26,43			20,14						
pka -C3 [02687]	26,92	26,930	0,0656	20,03	20,013	0,0208	1,003664	27,0286775	-0,669	0,66036302034636
pka -C3 [02687]	26,87			20,02						
pka -C3 [02687]	27,00			19,99						
pka-C3 [03065]	24,56	24,610	0,0436	19,95	19,950	0,0800	1,00685	24,7785898	1,5814102	2,668151692
pka-C3 [03065]	24,63			20,03						
pka-C3 [03065]	24,64			19,87					2,2500877	4,040431718

$E = 10^{(-1/slope)}$ slope= -3,724 E=1,86 pka-C3 primer pair

Figure 13:
Co-expression of Drosophila pka-C3 (03065) accelerates a TauP301L induced degenerative eye-phenotype in young flies whereas a knock-down of pka-C3 (02687) function has no impact on photoreceptor cell degeneration



Legend:

Re	Retina
La	Lamina
Me	Medulla

scale bar: 50µm

Figure 14:
Phosphorylation of Ser214 of TauP301L in flies co-expressing TauP301L and pka-C3 (02687) or pka-C3 (03065)

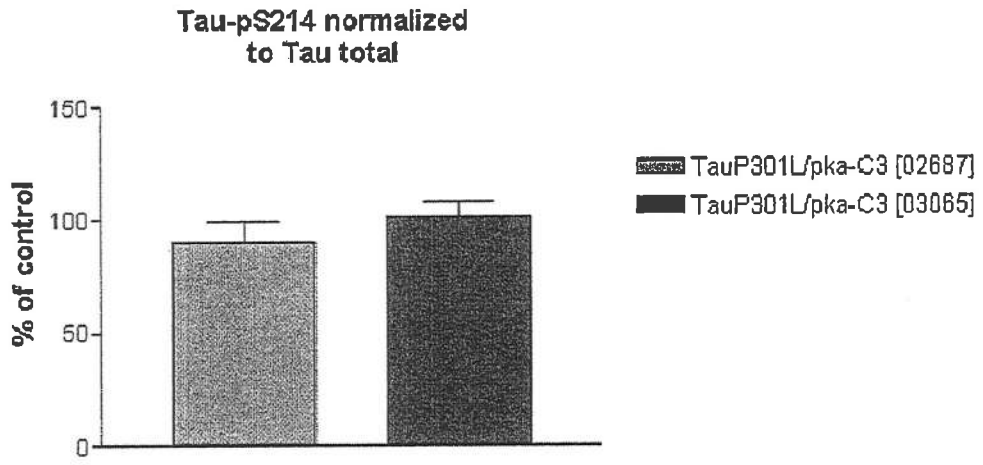
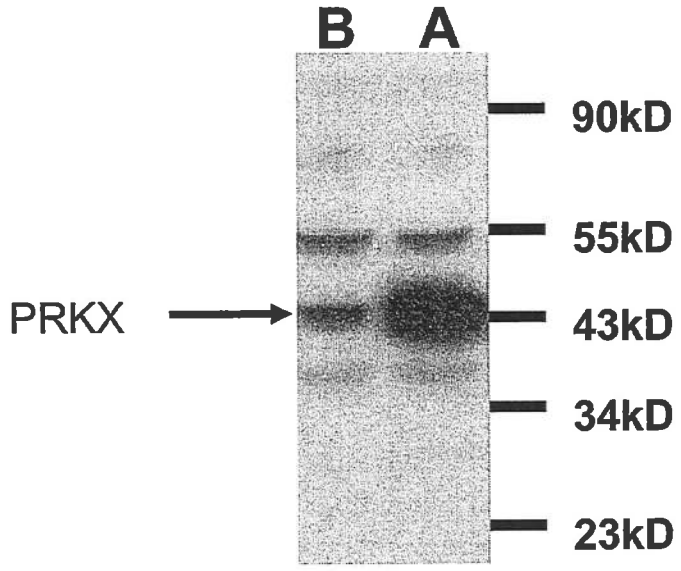


Figure 15: Westernblot analysis of inducible expression of PRKX in H4APPsw-tissue culture cells



A: H4 APPsw-PRKX-myc +tetracycline (induced)
B: H4 APPsw-PRKX-myc –tetracycline (control)

Figure 16: Immunofluorescence analysis of inducible expression of PRKX in H4APPsw-tissue culture cells

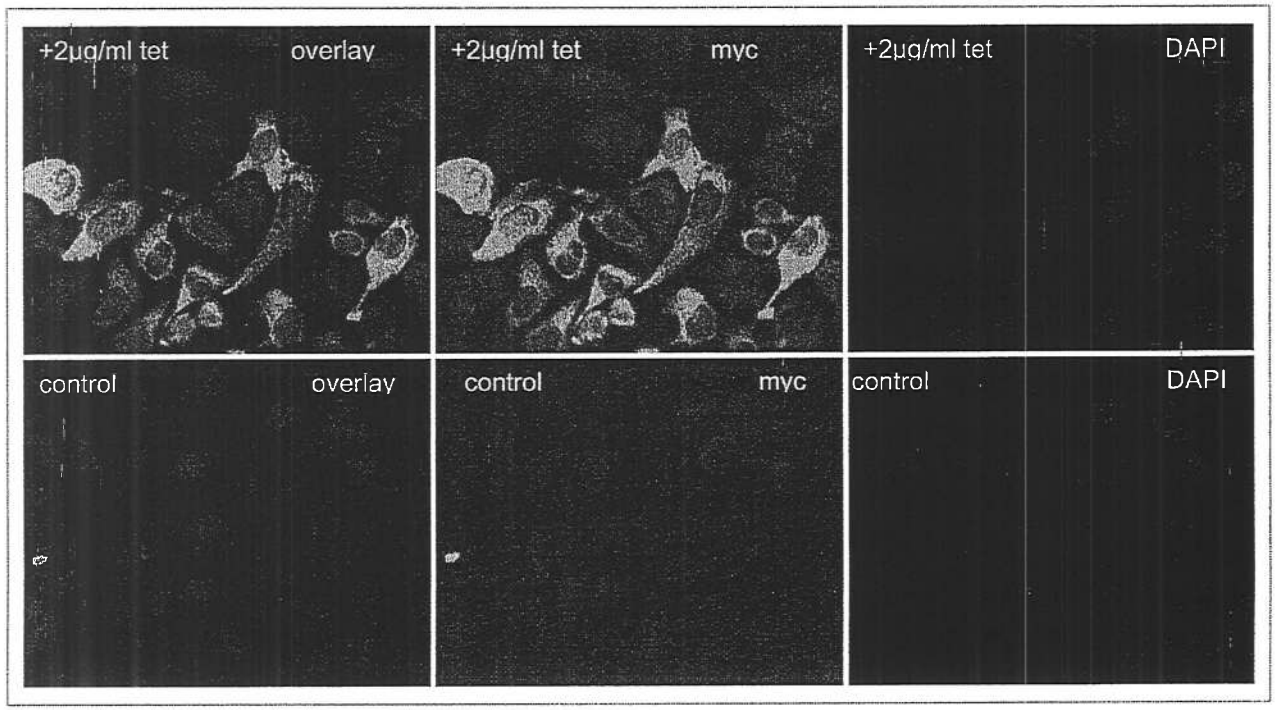


Figure 17: Targeting strategy for transgenic mice expressing human PRKX in neurons

