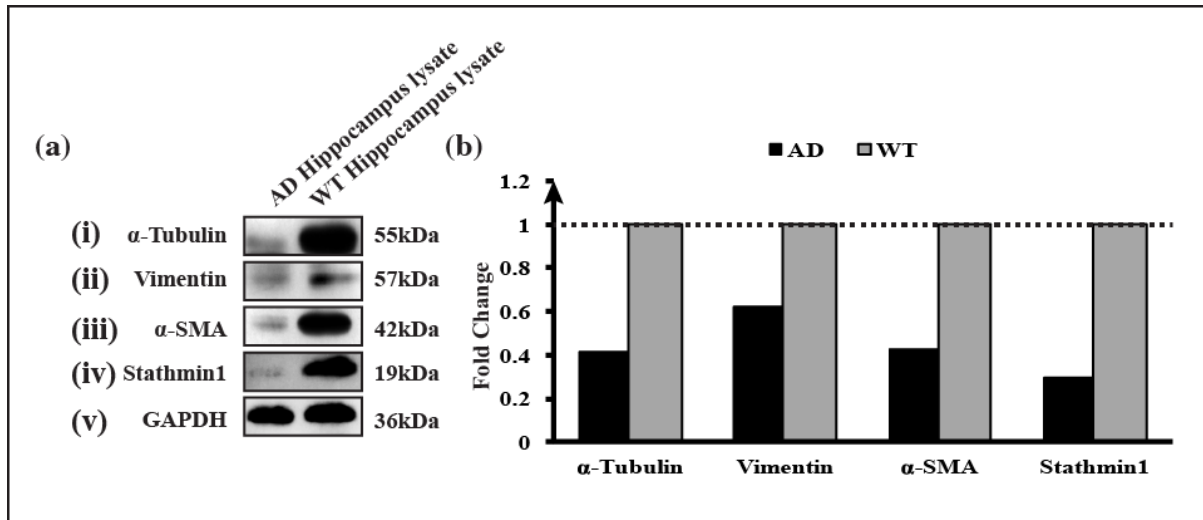
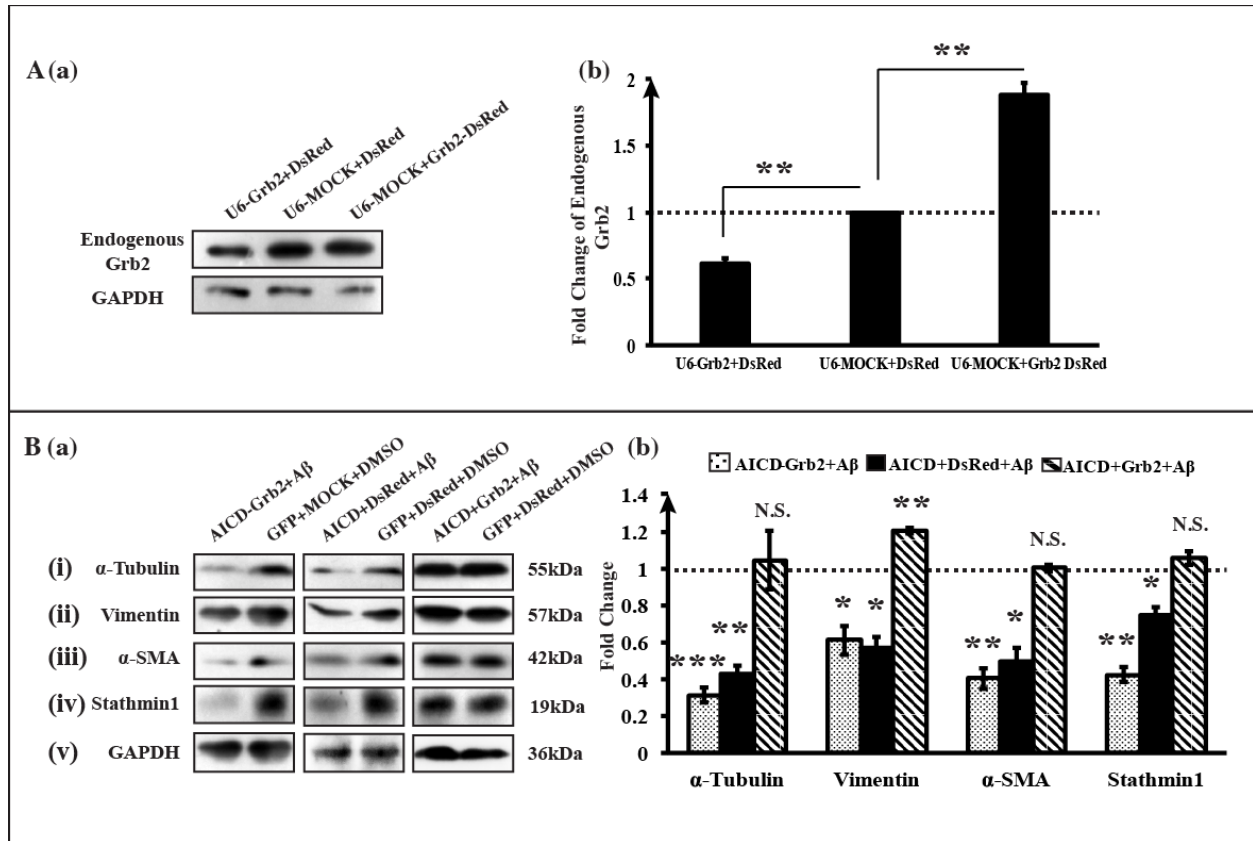


**Figure S1:**



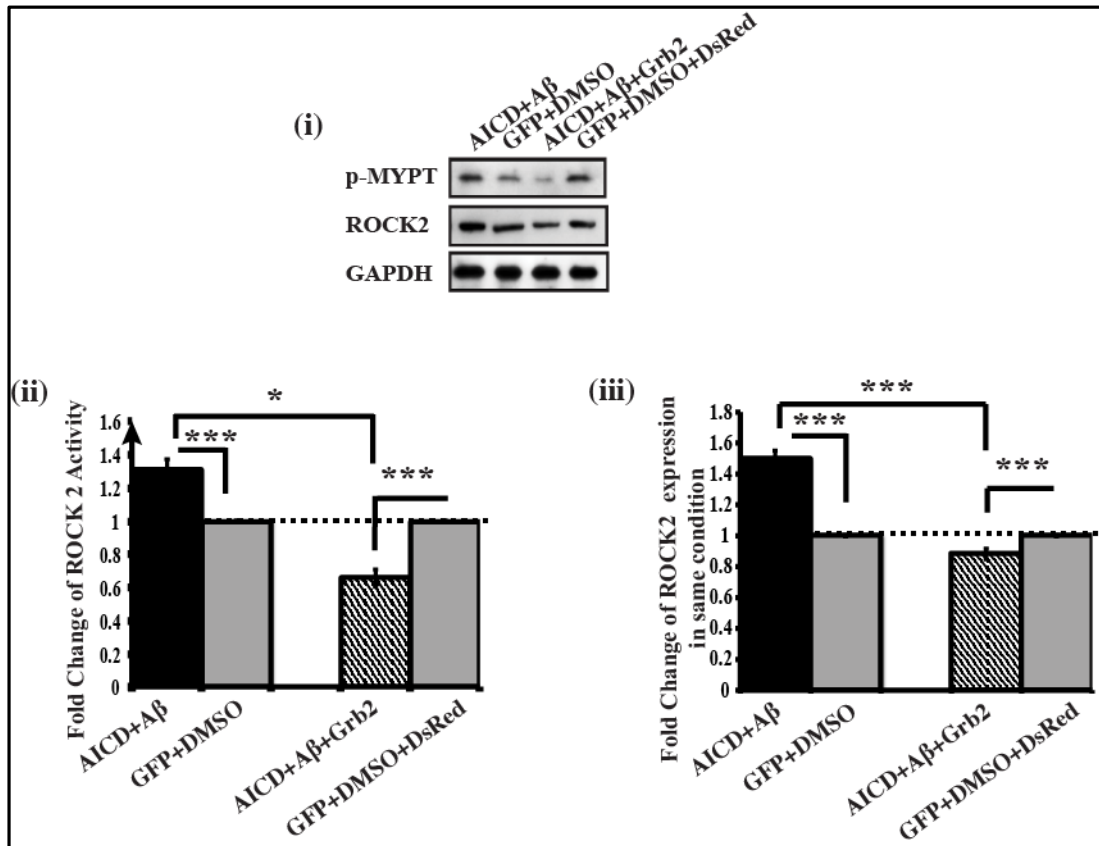
**Figure S1:**The expression levels of four cytoskeletal proteins viz.,  $\alpha$ -Tubulin, Vimentin,  $\alpha$ -Smooth muscle actin ( $\alpha$ -SMA) and Stathmin1 in Human hippocampus brain post-mortem tissue lysate of AD patients and Non-AD hippocampus brain (Wild Type) tissue lysates were compared by Western Blot. This result from a single experiment show similar trends of change as in case of AD whole brain lysate. **(a)** Depicts Western Blot of (n=1) four cytoskeletal proteins **(i)**  $\alpha$ -Tubulin, **(ii)** Vimentin, **(iii)**  $\alpha$ -SMA and **(iv)** Stathmin1 with **(v)** GAPDH used as internal control in AD hippocampus lysate compared to WT hippocampus lysate. **(b)** Bar diagram demonstrating the alterations in expression for  $\alpha$ -Tubulin, Vimentin,  $\alpha$ -SMA and Stathmin1.

**Figure S2:**



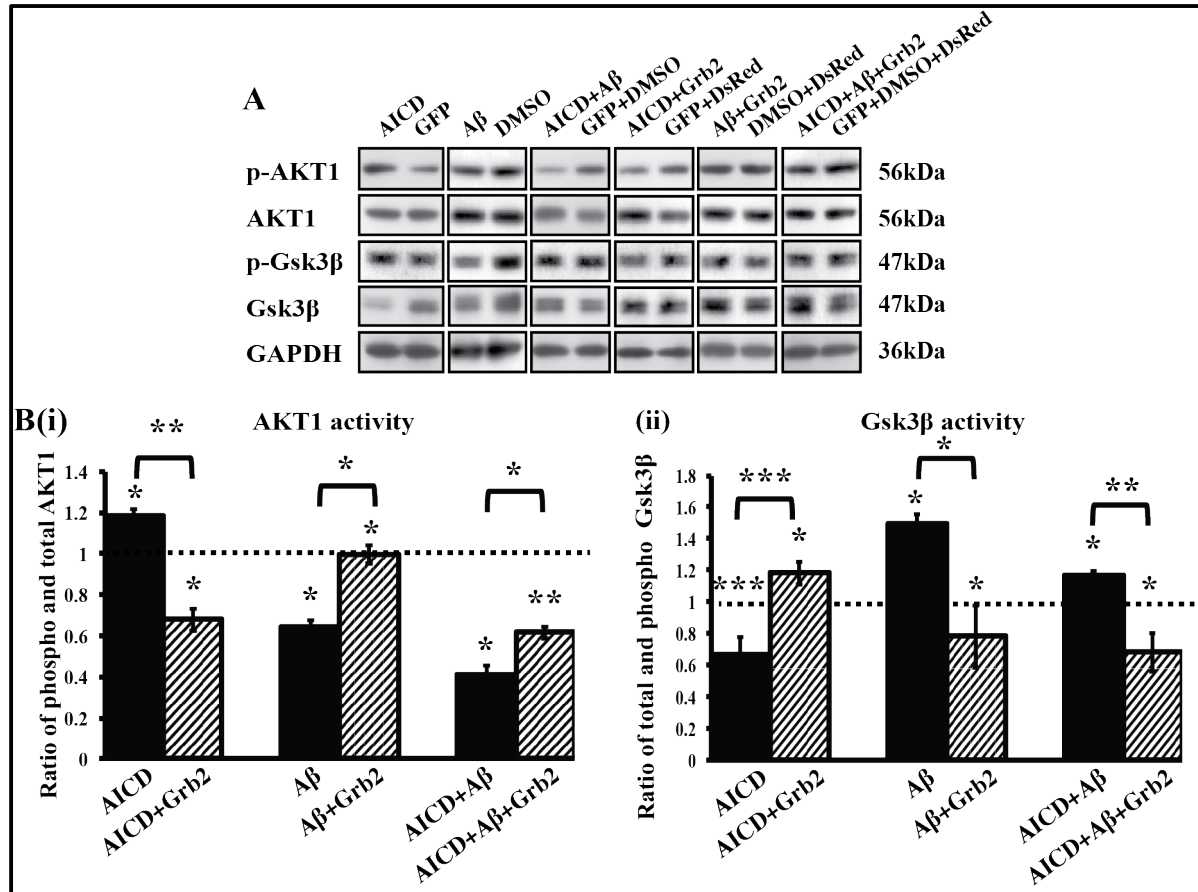
**Figure S2: Effect of Grb2 knock down.** **A(a)** demonstrates 60% lowering of endogenous Grb2 in Grb2 knock down cells where U6-Grb2 construct was transfected and compared to U6-MOCK and DsrRed transfected control cells. **(b)** Depicts the changes where Grb2-DsRed overexpressed cells show 87.9 % increase of endogenous Grb2 level. **B(a)** shows Western Blots where upon Grb2 knock down, the protein levels of **(a)(i)** α-Tubulin, **(ii)** Vimentin, **(iii)** α-SMA and **(iv)** Stathmin1 decreases significantly. **B(b)** shows alteration of cytoskeleton protein levels through bar diagrams.

**Figure S3:**



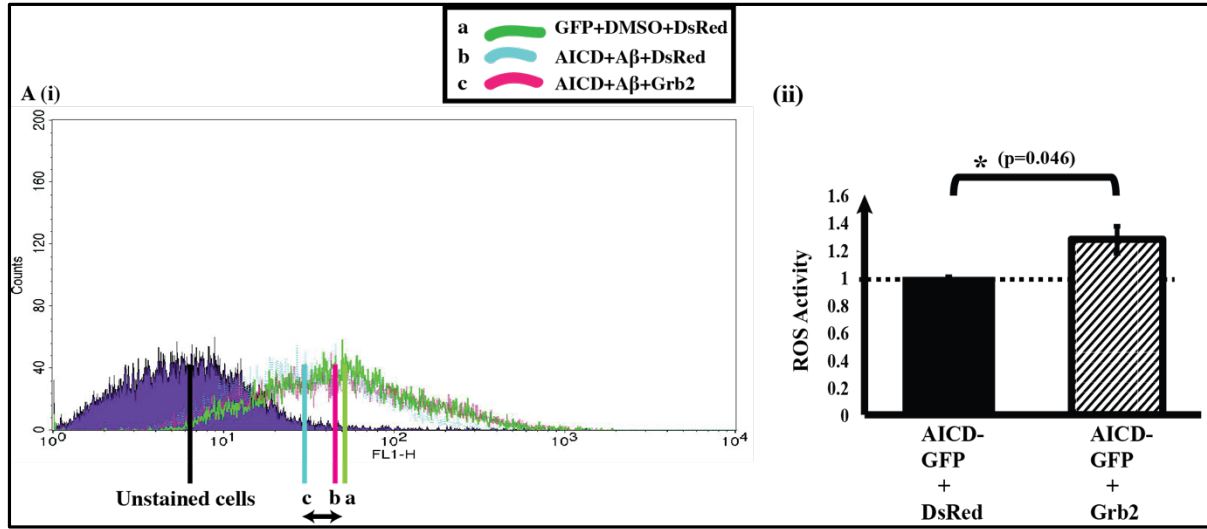
**Figure S3 (i)**, ROCK2 activity for both disease inducing condition (AICD and A $\beta$ ) and reversal condition (AICD,A $\beta$  and Grb2) compared to respective control conditions (GFP, DMSO;GFP, DMSO and DsRed). **(ii) and (iii)** show the histograms of activity change and expression level change of ROCK2, respectively.

Figure S4:



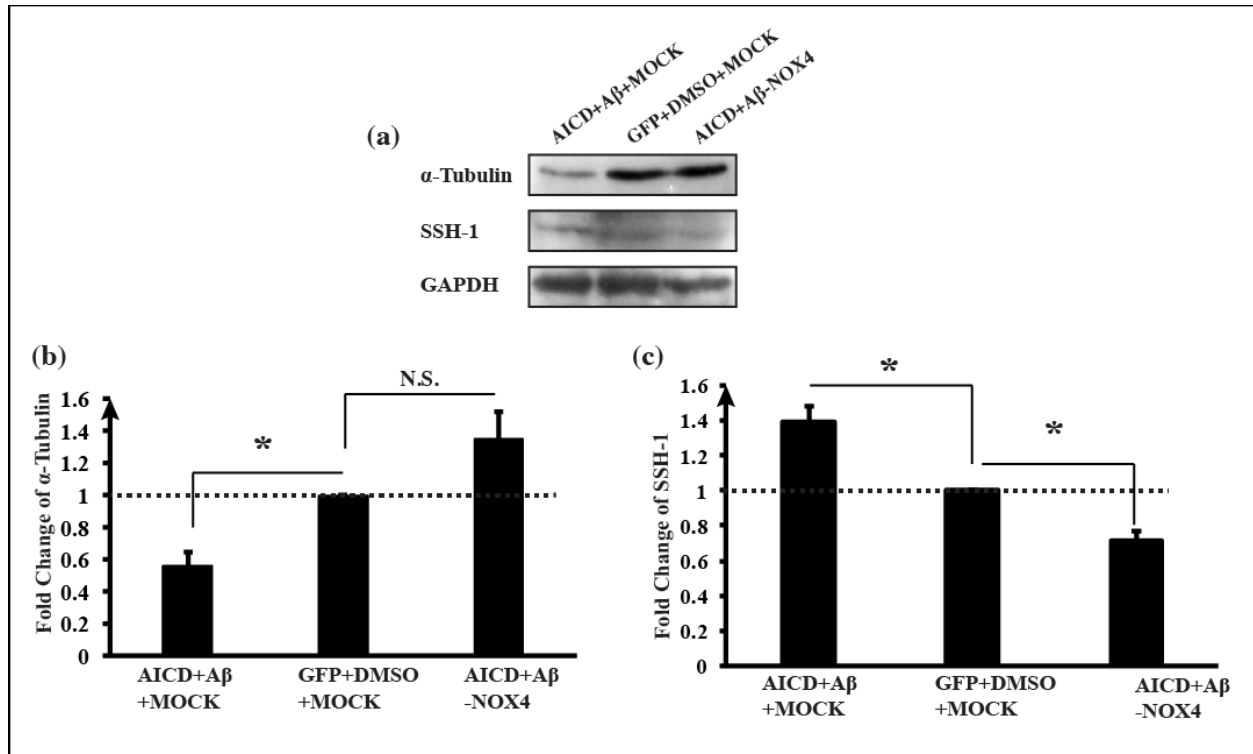
**Figure S4:** **A**, (i) shows the Western Blot to determine the alterations of Activities of both AKT1 and Gsk3β. AKT1 is activated through phosphorylation whereas Gsk3β is inactivated with Serine 9 (S9) phosphorylation. **B**, (i) and (ii) graphically shows the activity changes for both AKT1 and Gsk3β in presence of different conditions of AD inducing factors. AKT1 is activated in AICD transfected condition whereas Gsk3β is deactivated significantly. This observation corroborates with the classical assumption that AKT1 deactivates Gsk3β by S9 phosphorylation. However, Aβ and AICD+Aβ conditions significantly deactivates AKT1 thereby activating Gsk3β. From these observations, it is evident that AICD can neither activate Gsk3β nor can it deactivate AKT1 and Aβ would be indispensable for both.

**Figure S5:**



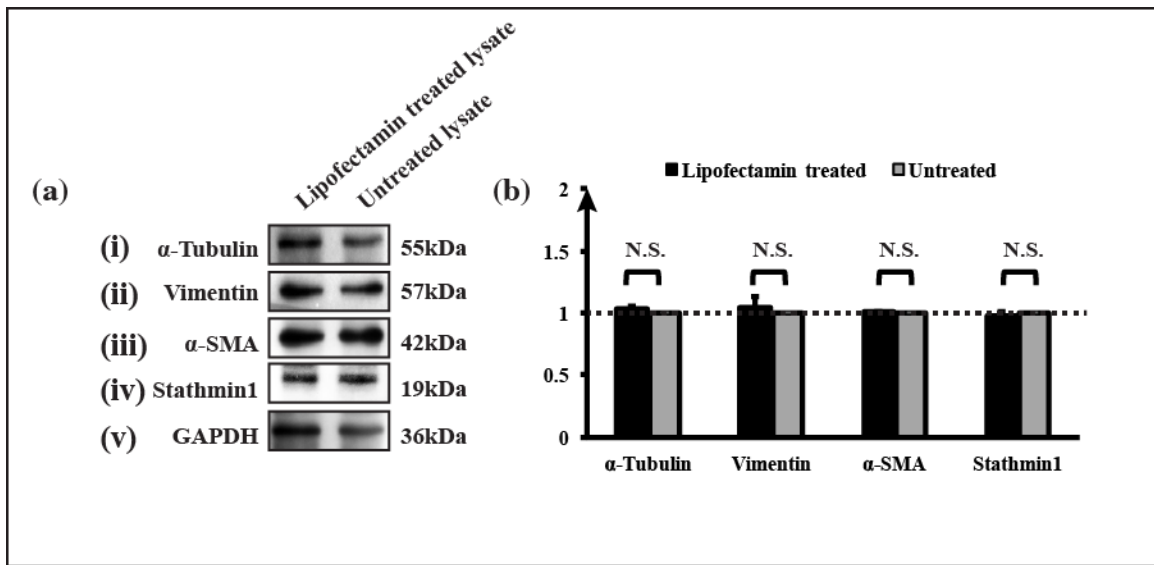
**Figure S5: ROS activity Assay.** **A(i)** shows the FACS data for ROS activity. ROS activities for both disease inducing condition (AICD, A $\beta$  and DsRed) and the reverse (AICD, A $\beta$  and Grb2) decreases compared to control (GFP, DMSO and DsRed). **(ii)** Shows graphically that ROS activity in presence of Grb2 increases significantly (\*;p=0.046; n=3).

**Figure S6:**



**Figure S6: Consequences of NOX4 knock down.** (a) shows the changes of protein levels of  $\alpha$ -Tubulin and Slingshot Homolog 1 (SSH-1) in both AD like condition (AICD and A $\beta$  treated cells with MOCK SiRNA) and AD like condition with NOX4 knock down situation (AICD and A $\beta$  treated cells with NOX4 SiRNA). (b) and (c) depicts the changes for both  $\alpha$ -Tubulin and SSH-1 respectively with 61.5% increase in  $\alpha$ -Tubulin and 28.46 % decrease in SSH-1.

**Figure S7:**



**Vehicle Control:** Cells were transfected with lipofectamin reagent and were checked for any effect on proteins of interest. We showed that lipofectamin treated cells had no significant effect compared to untreated cells. **(a)** Representative western blots of (n=3) four cytoskeletal proteins **(i)**  $\alpha$ -Tubulin, **(ii)** Vimentin, **(iii)**  $\alpha$ -SMA and **(iv)** Stathmin1 with **(v)** GAPDH used as internal control in lipofectamin treated lysate compared to untreated lysate. **(b)** Histograms showing changes in the four cytoskeletal proteins respectively. No significant changes could be seen.

**Table S1: Whole brain lysate chart**

Catalog number	Lot	Sex	Age	Ethnicity	Pathology
NB820-59177	C101138	M	98	Caucasian	Cause of death: Prostate Cancer
NB820-59177	B811092	F	60	Caucasian	Cause of death: unknown; had emphysema
NB820-59363	B909049	M	72	Caucasian	Alzheimer Disease
NB820-59363	B105129	M	75	Caucasian	Alzheimer Disease



**Table S2: Hippocampus brain lysate chart**

Catalog number	Lot	Age	Cause of death	Disease state
ab30181	GR190367-5	93	Lymphoma	Alzheimer's Brain Sample
ab30180	GR258239-1	82	Aortic Stenosis	Normal Brain Sample

**Table S3: Primer sequences and PCR conditions for qRT-PCR.**

Name of the genes	PCR condition	PCR Cycle	Primer sequences
<b><math>\alpha</math>-Tubulin (mouse)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward:5'GCAGTGTTTCGTAGACCTGGAA3' Reverse: 5'TTATTGGCAGCATCCTCCTT3'
<b>Vimentin (mouse)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward:5'ATGCTTCTCTGGCAGCTCTT3' Reverse: 5'AGTGAGGTCAGGCTTGAAAA3'
<b>Stathmin1 (mouse)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward:5'AGAAGGACCTTTCCTGGAG3' Reverse: 5' TTCTCATGCTCCCCGCTTC3'
<b>Grb2 (mouse)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward:5'AAATGCTCAGCAAACAGCGG3' Reverse: 5'TGAAGTGCTGCACATCATTTC3'
<b>GAPDH (mouse)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward:5'AGCCTCGTCCCCTAGACAAAA3' Reverse: 5'TGGCAACAATCTCCACTTTGC3'
<b><math>\alpha</math>-Tubulin (human)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward:5'CCGGGCAGTGTTGTAGACT3' Reverse: 5'GCAGCATCTTCTTTGCCTGT3'
<b>Vimentin (human)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward:5'GGCAGCTCTTGACCTTGAAC3' Reverse: 5'GTGAGGTCAGGCTTGAAAC3'
<b><math>\alpha</math>-SMA (human)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward: 5'ACCCAGCACCATGAAGATCA3' Reverse: 5'TTTGCGGTGGACAATGGAAG3'
<b>Stathmin1 (human)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward:5'AAGGATCTTTCCTGGAGGA3' Reverse: 5'GTTTCTCAGCCAGCTGCTTC3'
<b>Grb2 (human)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward:5'AGAAGTGGTACAAGGCAGAGC3' Reverse: 5'GATAAGAAAGCCCCATCGT3'
<b>GAPDH (human)</b>	95°C→10min[95°C 30sce, 55°C 30 sec, 60°C 1min] 72°C→10min	35	Forward:5'TCCCTGCACCACCAACTGTTAG3' Reverse: 5'GGCATGGCATGTGGTCATGAG3'