科技部補助專題研究計畫報告

以細胞、果蠅及動物模式探討咖啡酸改善第三型脊髓小腦運動失調症神經細胞凋亡及氧化壓力的功效及相關機制(第3年)

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本研究具有政策應用參考價值：■否 □是，建議提供機關
（勾選「是」者，請列舉建議可提供施政參考之業務主管機關）
本研究具影響公共利益之重大發現：□否 □是

中 華 民 國 109 年 10 月 11 日

中 文 摘 要 ： 第三型脊髓小腦運動失調症 (Spinocerebellar ataxia type 3，SCA3，又稱為Machado－Joseph disease)，為ataxin-3 蛋白質 polyglutatmine tract (polyQ)的麩醯胺酸重複個數突變引發的顯性遺傳神經退化疾病，目前無藥物可有效的控制脊髓小腦運動失調症發生。雖然polyQ 突變ataxin-3 蛋白質確切致病的機制仍不清楚，但是研究發現，除了polyQ 突變的ataxin-3 蛋白質會錯誤折疊蛋白質聚集在小腦與脊髓等特定神經細胞核內外， polyQ 突變 ataxin-3 蛋白質神經細胞基因轉錄、減少蛋白質分解作用、降低抗氧化物質及抗氧化酵素表現、與增加粒線體損傷和細胞凋亡相關分子表現等作用，致使神經細胞凋亡。食物中所含的植物素 (Phytochemicals)可經由增加神經細胞抗氧化和抗細胞凋亡作用，具有抑制神經退化之功效。咖啡酸 (Caffeic acid, CA) 廣泛存在於水果、蔬菜、酒、橄欖油及咖啡中，屬於hydroxycinnamic acid的酚酸類化合物 (Phenolic acids)，飲食中CA攝取量超過總酚酸類化合物90%。白藜蘆醇 (Resveratrol, Res) 屬於多酚類中stilbene類的化合物，主要食物來源包括紅葡萄、紅酒、莓果、堅果和花生等。雖然研究已證實CA和Res具有良好的抗氧化及抗神經毒殺的功效，但是CA和Res是否具有減緩SCA3 神經退化病程發展的保健功效尚未清楚。本論文以基因轉殖表現polyQ突變ataxin-3蛋白質的SK-N-SH-MJD78神經細胞株與 ELAV-SCA3tr-Q78果蠅模式，評估CA和Res的神經保護角色及可能機制。研究結果證實CA和Res可降低氧化劑tert-butyl hydroperoxide (tBH)誘發SK-N-SH-MJD78神經細胞株細胞凋亡。此外，CA和Res可增加SK-N-SH-MJD78細胞抗氧化及自噬作用相關蛋白質表現，並且降低活性氧化物 (Reactive oxygen species, ROS)、polyQ突變ataxin-3蛋白質和細胞中聚集蛋白質表現量。進一步發現，餵食CA和Res有助於改善ELAV-SCA3tr-Q78果蠅的爬行能力與存活率。CA和Res亦可改善ELAV-SCA3tr-Q78果蠅腦部ROS、polyQ突變ataxin-3蛋白質及與細胞凋亡、抗氧化與自噬作用相關蛋白質表現。在SK-N-SH-MJD78細胞，利用reporter gene assay、暫時性轉殖dominant-negative mutant IκB-α 質體與siNrf2等實驗證實CA和Res對SCA3的神經保護作用與其降低p53與增加NF-κB及Nrf2轉錄活性有關。此研究結果，除可了解CA和Res

中 文 關 鍵 詞 ： polyQ 突變ataxin-3 蛋白質、咖啡酸、細胞凋亡、抗氧化能力

英 文 摘 要 ： Spinocerebellar ataxia type 3 (SCA3, also called Machado－Joseph disease (MJD), a late-onset and fatally inherited neurodegenerative disease, is caused by an abnormal expansion of the polyglutamine (polyQ) repeat in the protein ataxin-3. Until now, there is no established disease-modifying therapeutic strategy has been available for SCA3. Although the exact mechanism is unknown, the pathogenic effects of polyQ expanded mutant ataxin-3 protein are associated with not only misfolding and aggregation in nuclei of specific neurons but also dysregulation of transcription, protein degradation, mitochondrial function, apoptosis, and antioxidant potency and these thus trigger neuronal death. It is well

established that phytochemicals in food through antioxidant and anti-apoptotic effects on neurons exert valuable therapeutic benets in neurodegenerative diseases. Caffeic acid (CA), widely present in various agricultural products such as fruits, vegetables, wine, olive oil, and coffee, classified as a phenolic compounds of hydroxycinnamic acid and accounts for almost 90% of total phenolic acid intake in the diet. Resveratrol (Res), a polyphenolic stilbene, is present in variety of dietary sources such as red grapes, red wine, berries, nuts and peanuts. Although data have shown the antioxidant and antineurotoxic properties of CA and Res, the health effects of CA and Res against neurodegenerative progress in SCA3 is unknown. Here we investigated the protective role and possible mechanisms of CA and Res in SK-N-SH-MJD78 neuroblastoma cells and ELAV-SCA3tr-Q78 transgenic ies expressing mutant ataxin-3 and mutant ataxin-3 polyQ tract, respectively. Our data showed that CA and Res decreased apoptosis in the pro-oxidant tert-butyl hydroperoxide (tBH)-treated SK-N-SH-MJD78 cells. Moreover, treatments with CA and Res increased the levels of antioxidant and autophagy protein expression as well as diminished ROS, and expression and aggregation of mutant ataxin-3 in SK-N-SH-MJD78 cells. We further discovered that supplementations with CA and Res enhanced survival and motor performance in ELAV-SCA3tr-Q78 transgenic ies. CA and Res also diminished ROS, mutant ataxin-3 polyQ tract, and apoptotic-related molecules, as well as increased antioxidant and autophagy molecules in brain of ELAV-SCA3tr-Q78 transgenic ies. Notably, in SK-N-SH-MJD78 cells, using reporter gene assay, transfection experiments with a dominant-negative mutant IκB-α (DNM IκB-α) plasmid and Nrf2 siRNA demonstrated that the neuroprotective effects of CA and Res on SCA3 are through modulating transcriptional activity of p53, NF-κB and Nrf2. In summary, our findings demonstated the neuroprotective effect and possible mechanisms of CA and Res in improving mutant ataxin-3 induced ROS production and neuronal apoptosis. Moreover, these data could provide information for the preclinical studies of CA and Res in modulating neurodegenerative progression in SCA3.

英文關鍵詞：polyQ expanded mutant protein ataxin-3, Cafffeic acid, Cell apoptosis, Antioxidative capacity

Treatment with Caffeic Acid and Resveratrol Alleviates Oxidative Stress Induced Neurotoxicity in Cell and Drosophila Models of Spinocerebellar Ataxia Type3

Abstract

Spinocerebellar ataxia type 3 (SCA3) is caused by the expansion of a polyglutamine (polyQ) repeat in the protein ataxin-3 which is involved in neuronal death. Here we show that caffeic acid (CA) and resveratrol (Res) decreased reactive oxygen species (ROS), mutant ataxin-3 and apoptosis and increased autophagy in t-butyl hydroperoxide (tBH)-treated SK-N-SH-MJD78 cells containing mutant ataxin-3. Furthermore, CA and Res improved survival and locomotor activity and decreased mutant ataxin-3 and ROS levels in tBH-treated SCA3 *Drosophila*. CA and Res also altered p53 and nuclear factor-κB (NF-κB) activation and expression in tBH-treated cell and fly models of SCA3, respectively. Blockade of NF-κB activation annulled the protective effects of CA and Res on apoptosis, ROS, and p53 activation in tBH-treated SK-N-SH-MJD78 cells, which suggests the importance of restoring NF-κB activity by CA and Res. Our findings suggest that CA and Res may be useful in the management of neuronal apoptosis in SCA3.

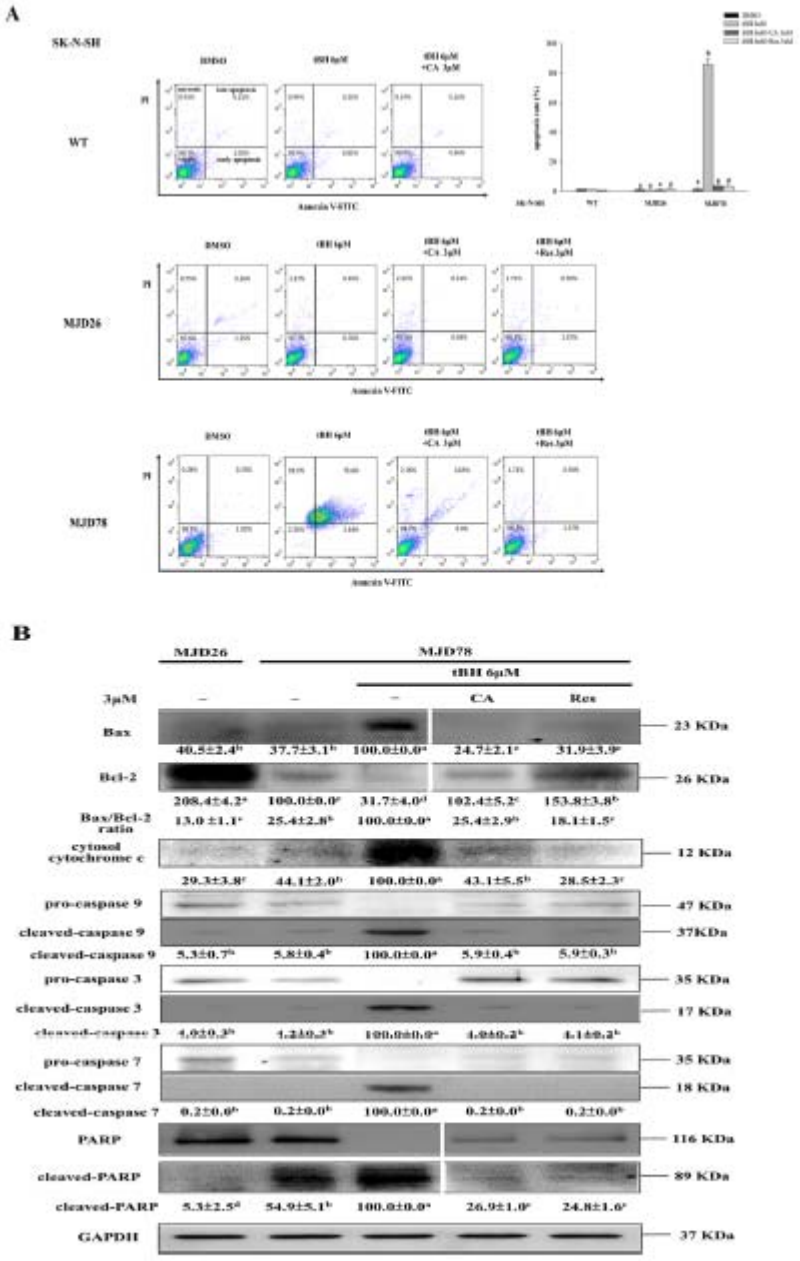
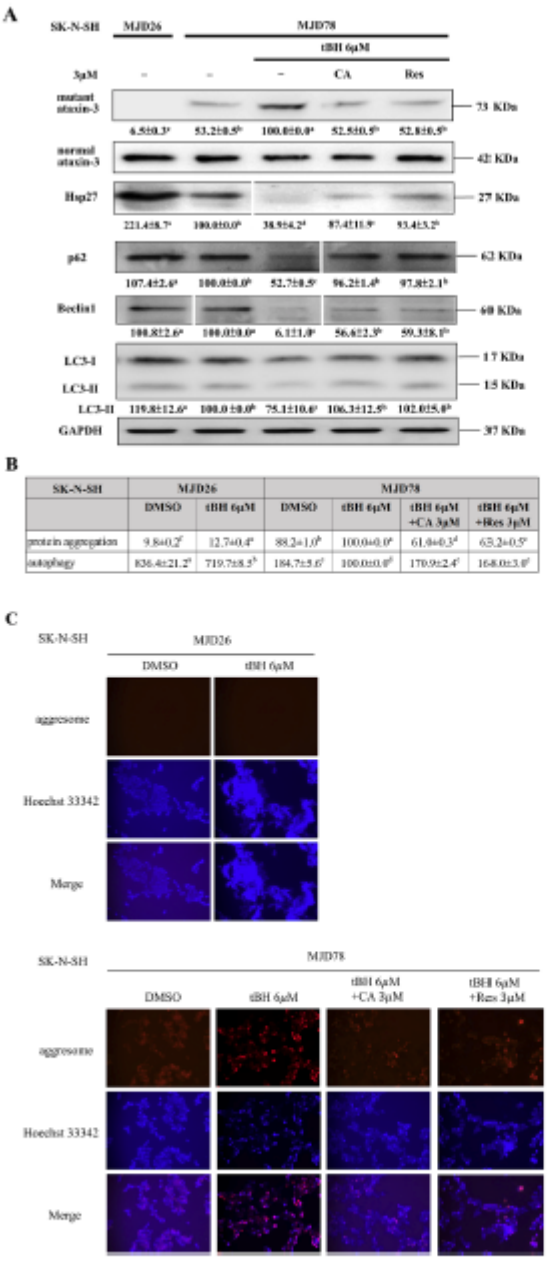


Figure 1. Effects of CA and Res on tBH-induced apoptosis in SK-N-SH WT, SK-N-SH-MJD26, and SK-N-SH-MJD78 cells. **(A)** Cell apoptosis was measured by flow cytometry (48-h treatment). Bar graph is presented as the percentage of early and late apoptosis defined as annexin V+/PI− and annexin V+/PI+. **(B)** Protein expression of Bax, Bcl-2, cytosolic cytochrome *c*, and pro and cleaved caspase 3, 7, 9, and PARP (24-h treatment). Data are mean ± SD and are expressed as the percentage of SK-N- SH-MJD78 cells treated with tBH alone. Values not sharing the same letter are significantly different ($p < 0.05$).

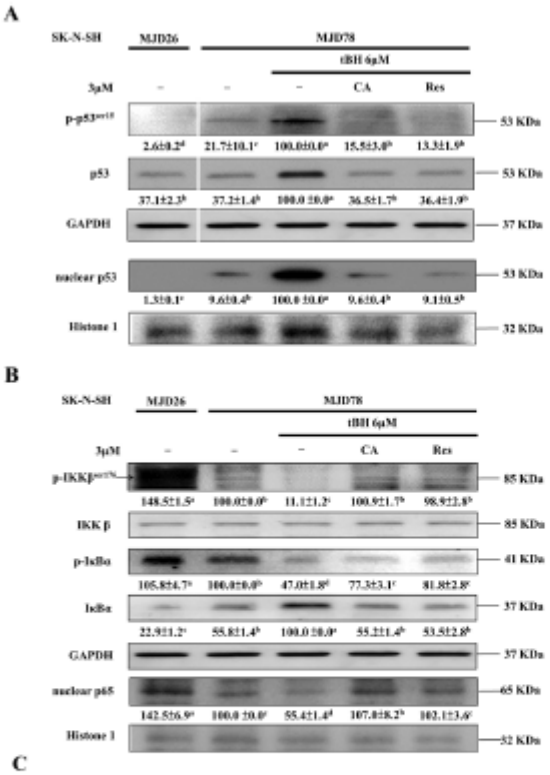
	WT				MJD26				MJD78			
SK-N-SH	DMSO	tBH 6 μM	tBH 6 μM + CA 3 μM	tBH 6 μM + Res 3 μM	DMSO	tBH 6 μM	tBH 6 μM + CA 3 μM	tBH 6 μM + Res 3 μM	DMSO	tBH 6 μM	tBH 6 μM + CA 3 μM	tBH 6 μM + Res 3 μM
MTT[a]	100.0 ± 0.0	94.5 ± 0.4	95.4 ± 0.3	95.5 ± 0.4	100.0 ± 0.0	99.8 ± 0.1	96.6 ± 0.3	99.1 ± 0.1	100.0 ± 0.0	43.4 ± 0.3	96.5 ± 0.2	94.7 ± 0.3
H_2DCFDA[a]	4.5 ± 1.7[a]	7.9 ± 3.7[ab]			4.9 ± 1.4[ab]	6.6 ± 3.3[ab]			10.6 ± 0.3[bcd]	100.0 ± 0.0[a]	15.1 ± 3.4[b]	12.1 ± 2.3[bc]
MitoSOX[a]	0.8 ± 0.0[c]	0.7 ± 0.0[c]			0.8 ± 0.1[c]	0.8 ± 0.1[c]			4.3 ± 0.4[b]	100.0 ± 0.0[a]	4.1 ± 0.6[b]	4.4 ± 1.2[b]
TMRE[a]					4542.0 ± 13.5[a]				1552.0 ± 98.5[b]	100.0 ± 0.0[d]	1148.2 ± 3.0[c]	1150.1 ± 94.9[c]
caspase 3 activity[a]					8.6 ± 0.9[a]				32.1 ± 1.7[b]	100.0 ± 0.0[a]	28.7 ± 0.4[b]	45.6 ± 0.6[a]

Table 1. Effects of CA and Res on MTT assay, ROS, mitochondrial transmembrane potential and caspase 3 activity on tBH treated SK-N-SH WT, SK-N-SH-MJD26 and SK-N-SH-MJD78 cells[a]. [a]SK-N-SH WT, SK-N-SH-MJD26 and SK-N-SH-MJD78 cells were treated with or without tBH (6 μM) plus DMSO vehicle control, CA, Res (3 μM) for 48 h (MTT assay) or for 1 h (H2DCFDA) or for 3 h (MitoSOX or TMRE) or for 24 h (caspase-3 activity). Data are the mean ± SD of at least four separate experiments. [b]Data are expressed as the percentage of the SK-N-SH-MJD78 cells treated with tBH alone and values in the same row with different superscript letters are significantly different ($p < 0.05$). [c]Within same cell type, data are expressed as the percentage of cells treated with DMSO alone and values with different superscript letters are significantly different ($p < 0.05$).



SK-N-SH	MJD26		MJD78			
	DMSO	tBH 6μM	DMSO	tBH 6μM	tBH 6μM +CA 3μM	tBH 6μM +Res 3μM
protein aggregation	9.8±0.2ᶠ	12.7±0.4ᵉ	88.2±1.0ᵇ	100.0±0.0ᵃ	61.0±0.3ᵈ	65.2±0.5ᶜ
autophagy	836.4±21.2ᵉ	719.7±8.5ᵇ	184.7±5.6ᶠ	100.0±0.0ᵍ	170.9±2.4ᶠ	164.0±3.0ᶠ

Figure 2. Effects of CA and Res on levels of mutant ataxin-3 and Hsp27, protein aggregates, and autophagy in tBH-treated SK-N-SH-MJD78 cells. After 24-treatment (**A**) Mutant and normal ataxin-3, Hsp27, p62, Beclin1, and LC3 protein expression were measured by Western blot analysis (**B**) Levels of Protein aggregates and autophagy stained by using aggregation assay, and acridine orange staining, respectively were quantified by flow cytometric analysis. (**C**) The images of protein aggregates were detected by ProteoStat Aggresome Detection Kit (Enzo Life Science (red). Cell nuclei were stained with Hoechst 33342 (blue). Data are the mean ± SD of at least four separate experiments and are expressed as the percentage of SK-N-SH-MJD78 cells treated with tBH alone. Values not sharing the same letter are significantly different ($p < 0.05$).



C

SK-N-SH	MJD26	MJD78			
	DMSO	DMSO	tBH 6μM	tBH 6μM +CA 3μM	tBH 6μM +Res 3μM
NF-κB luciferase activity	314.7±4.8d	197.8±4.8b	100.0±0.0f	187.5±6.6b	190.2±6.3b
p53 luciferase activity	3.1±0.5d	22.4±1.2c	100.0±0.0f	33.3±3.2b	25.5±2.1c

Figure 3. Effects of CA and Res on activation of p53 and NF-κB in tBH-treated SK-N-SH-MJD78 cells. **(A)** and **(B)** Protein expression of phosphorylated and total p53, IKK-β, IκB-α, and nuclear p53 and p65. **(C)** NF-κB and p53 reporter gene activities (3-h and 4-h treatments for p53 and NF-κB activation, respectively). Data are the mean ± SD and are expressed as the percentage of SK-N-SH-MJD78 cells treated with tBH alone. Values not having the same letter are significantly different ($p < 0.05$).

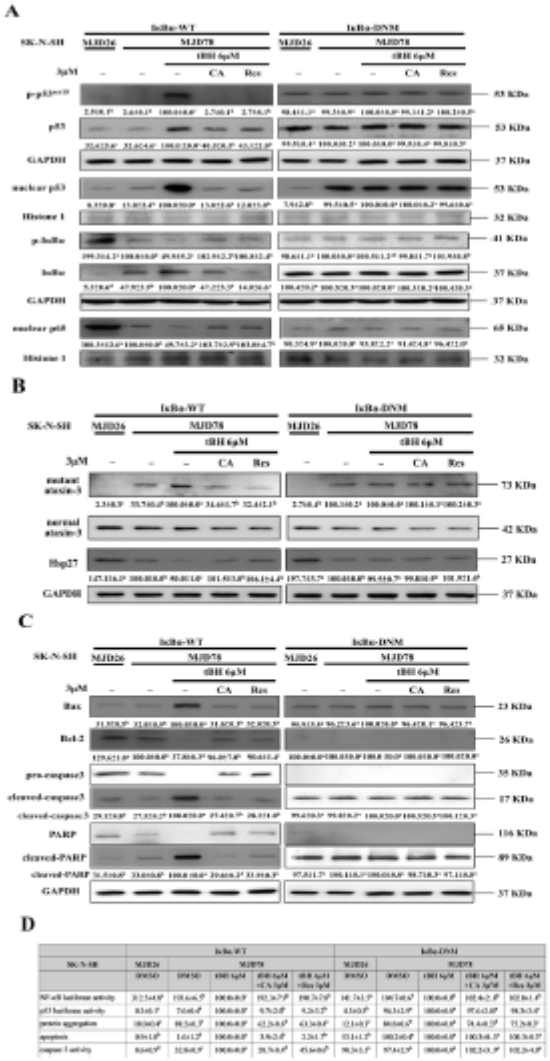


Figure 4. Effects of CA and Res in tBH-treated SK-N-SH-MJD78 cells transfected with dominant-negative mutant IκB-α. Cells were transiently transfected with IκB-α wild-type (WT) or DNM IκB-α as well as with or without reporter genes of p53-Luc or pNF-κB-Luc for 16 h and were then treated with either vehicle control or tBH plus CA or Res. **(A)** Phosphorylated and total p53 and IκB-α as well as nuclear p53 and p65 (3-h and 4-h treatments for p53 and NF-κB activation, respectively). **(B)** Protein expression of mutant and normal ataxin-3 and Hsp27. **(C)** Protein expression of Bax, Bcl-2, and pro and cleaved caspase 3 and PARP. **(D)** Levels of NF-κB and p53 reporter gene activities, protein aggregates, cell apoptosis rates, and caspase 3 activity. Data are the mean ± SD. Within treatments with the same plasmid transfection, data are expressed as the percentage of the SK-N-SH-MJD78 cells treated with tBH alone, and values not having the same letter are significantly different ($p < 0.05$).

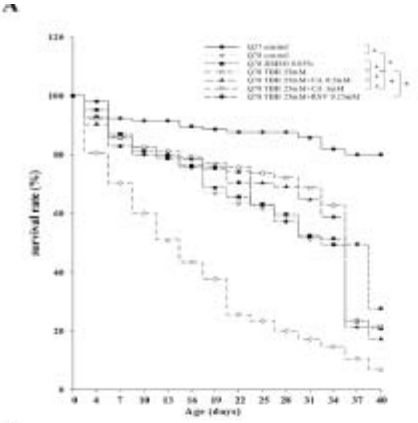


Figure 5. Effects of CA and Res on survival rates and climbing activity in tBH-treated ELAV-SCA3tr-Q78 transgenic *Drosophila*. **(A)** Survival rates were plotted and compared across groups by use of Kaplan-Meier log-rank analysis. The mean life span and SD are shown, $^{*}p < 0.01$ (n = 300). **(B)** Climbing activity (%) was calculated as $N_{top}/N_{total} \times 100$, where N_{total} and N_{top} represent the number of total flies and the number of flies at the top (over the 5-cm line), respectively. Within the same age, values not sharing the same letter are significantly different ($p < 0.05$).

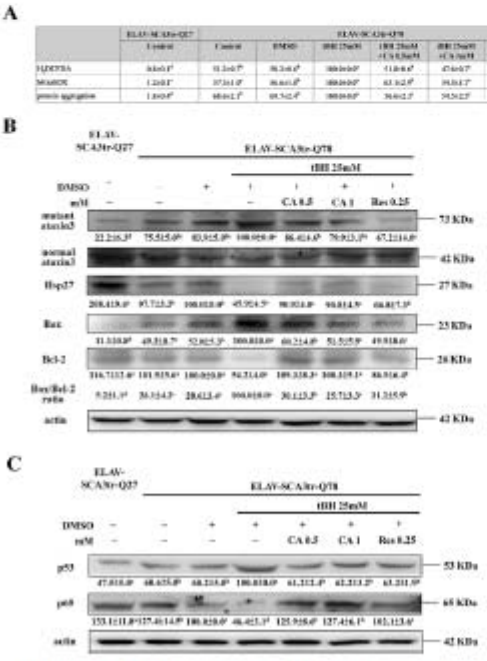


Figure 6. Effects of CA and Res on tBH-treated ELAV-SCA3tr-Q78 transgenic *Drosophila*. **(A)** H_2DCFDA, MitoSOX, and protein aggregate levels. **(B)** Mutant and normal ataxin-3, Hsp27, Bax, Bcl-2. **(C)** p53 and NF-κB protein expression in 22-day-old male ELAV-SCA3tr-Q78 flies. Values are mean ± SD, n = 50 male flies in three separate experiments. Data are expressed as the percentage of ELAV-SCA3tr-Q78 flies treated with tBH alone. Values not having the same letter are significantly different ($p < 0.05$).

Caffeic acid and resveratrol ameliorate cellular damage in cell and Drosophila models of spinocerebellar ataxia type 3 through upregulation of Nrf2 pathway

Abstract

Polyglutamine (polyQ)-expanded mutant ataxin-3 protein, which is prone to misfolding and aggregation, leads to cerebellar neurotoxicity in spinocerebellar ataxia type 3 (SCA3), an inherited PolyQ neurodegenerative disease. Although the exact mechanism is unknown, the pathogenic effects of mutant ataxin-3 are associated with dysregulation of transcription, protein degradation, mitochondrial function, apoptosis, and antioxidant potency. In the present study we explored the protective role and possible mechanism of caffeic acid (CA) and resveratrol (Res) in cells and *Drosophila* expressing mutant ataxin-3. Treatment with CA and Res increased the levels of antioxidant and autophagy protein expression with consequently corrected levels of reactive oxygen species, mitochondrial membrane potential, mutant ataxin-3, and the aggregation of mutant ataxin-3 in SK-N-SH-MJD78 cells. Moreover, in SK-N-SH-MJD78 cells, CA and Res enhanced the transcriptional activity of nuclear factor erythroid-derived-2-like 2 (Nrf2), a master transcription factor that upregulates the expression of antioxidant defense genes and the autophagy gene p62. CA and Res improved survival and motor performance in SCA3 *Drosophila*. Additionally, the above-mentioned protective effects of CA were also observed in CA-supplemented SCA3 *Drosophila*. Notably, blockade of the Nrf2 pathway by use of small interfering RNA annulled the health effects of CA and Res on SCA3, which affirmed the importance of the increase in Nrf2 activation by CA and Res. Additional studies are need to dissect the protective role of CA and Res in modulating neurodegenerative progression in SCA3 and other polyQ diseases.

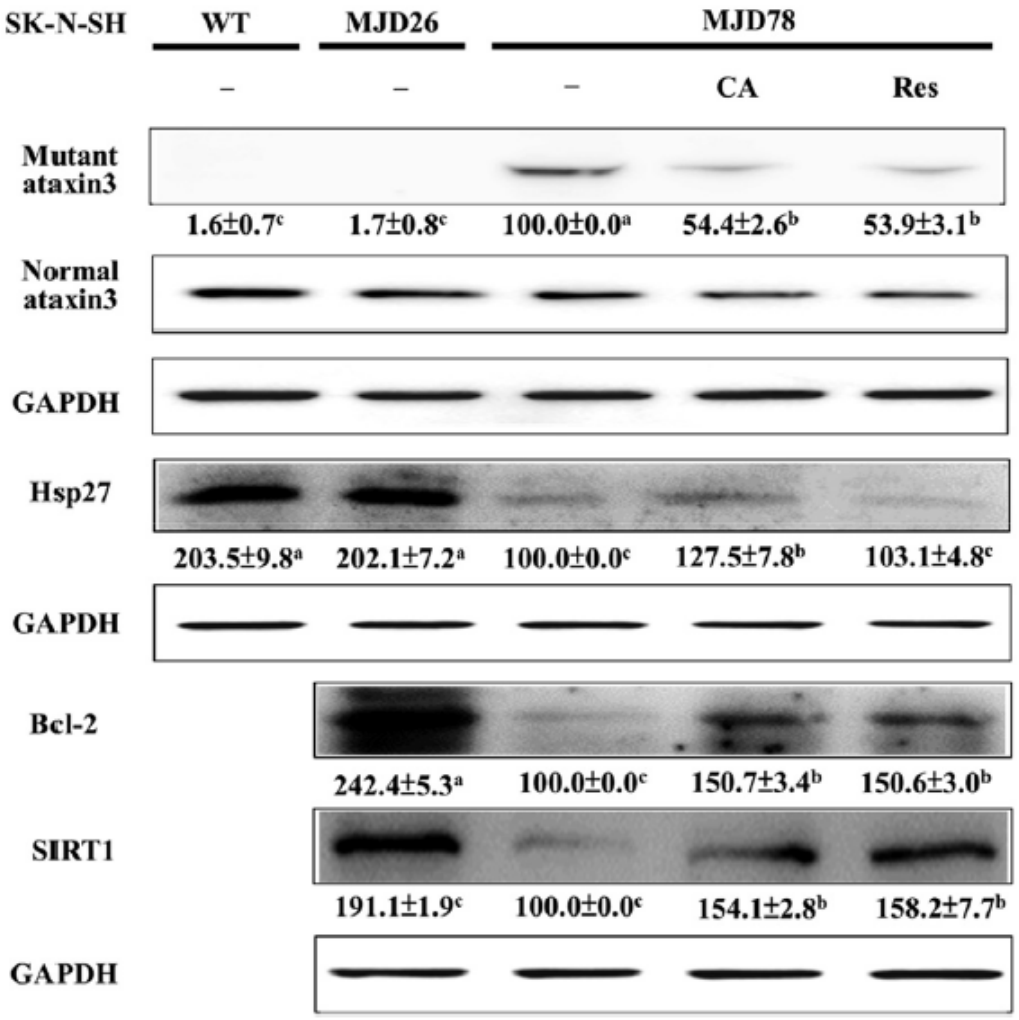


Fig. 1. Effects of CA and Res on protein expression of mutant ataxin-3, Hsp27, Bcl-2 and SIRT1 in SK-N-SH-MJD78 cells. SK-N-SH-WT, SK-N-SH-MJD26, and SK-N-SH-MJD78 cells were treated with or without DMSO vehicle control or 3 μM CA or Res for 24 h. Data are means ± SD of at least three separate experiments and are expressed as the percentage of SK-N-SH-MJD78 cells treated with the vehicle control. Values not sharing the same letter are significantly different ($P < 0.05$).

Table 1
Effects of CA and Res on cell viability (MTT assay), protein aggregation and MMP (TMRE staining) in SK-N-SH-MJD78 cells*.

SK-N-SH	WT	MJD26	MJD78		
	DMSO	DMSO	DMSO	CA	Res
MTT#	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	96.4 ± 0.2	92.6 ± 0.2
protein aggregation#	8.0 ± 0.5^{e}	14.0 ± 1.4^{d}	100.0 ± 0.0^{a}	65.6 ± 2.1^{c}	73.0 ± 1.7^{b}
TMRE#	NT	360.4 ± 4.2^{a}	100.0 ± 0.0^{c}	245.4 ± 2.6^{b}	241.3 ± 1.6^{b}

* SK-N-SH-WT, SK-N-SH-MJD26, and SK-N-SH-MJD78 cells were treated with or without DMSO vehicle control or 3 μM CA or Res for 24 h except for measurement of the MMP level (4 h treatment).

Values are expressed as the percentage of SK-N-SH-MJD78 cells treated with the vehicle control. Data are means ± SD of at least three separate experiments and not sharing the same letter are significantly different ($P < 0.05$). NT: not tested.

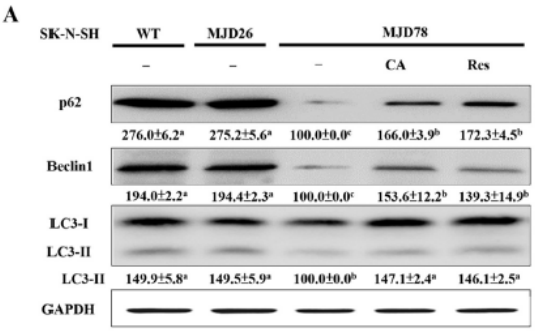
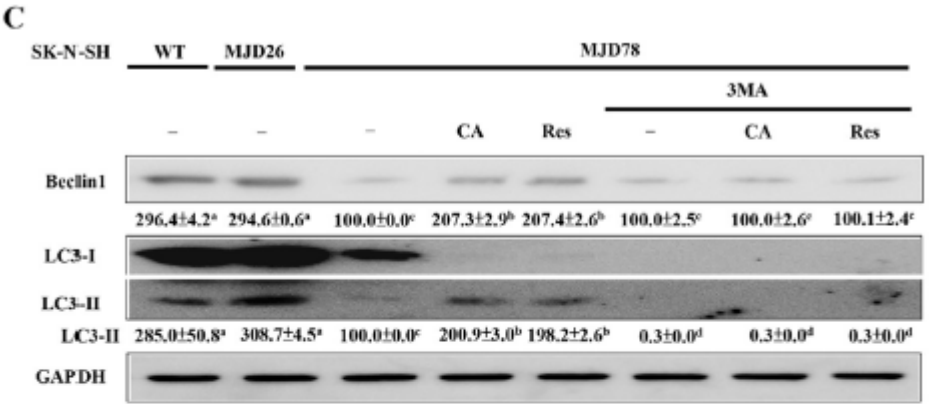


Fig. 2. Effects of CA and Res on autophagy in SK-N-SH-MJD78 cells. Cells were treated with or without DMSO vehicle control or 3 μM CA or Res for 24 h in the absence or presence of pretreatment with 1 mM 3MA for 1 h. (A) and (C) Protein expression of p62, Beclin-1, and LC3-II. (B) Autophagic cells and protein aggregation were measured by acridine orange staining and the PROTEOSTAT® protein aggregation assay, respectively, and were quantified by flow cytometry. (D) Protein expression of mutant and normal ataxin-3. Values are expressed as the percentage of SK-N-SH-MJD78 cells treated with the vehicle control. Data are means ± SD of at least three separate experiments and not sharing the same letter are significantly different ($P < 0.05$).

B

SK-N-SH	WT	MJD26	MJD78					
						3MA		
	DMSO	DMSO	DMSO	CA	Res	DMSO	CA	Res
autophagy	503.8±14.4^{a}	505.6±21.8^{a}	100.0±0.0^{c}	355.5±15.5^{b}	340.8±19.3^{b}	97.7±1.1^{c}	98.0±1.5^{c}	98.9±1.0^{c}
protein aggregation	7.6±0.4^{e}	14.2±0.2^{d}	100.0±0.0^{b}	64.7±0.7^{c}	70.7±0.8^{b}	102.6±1.3^{a}	103.4±1.8^{a}	102.8±1.6^{a}



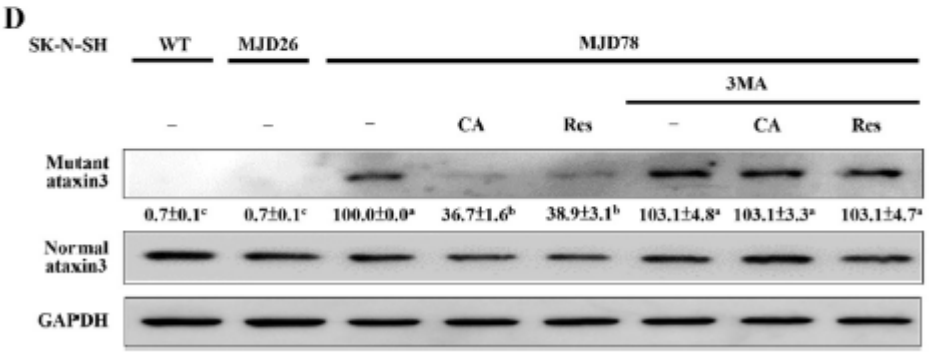
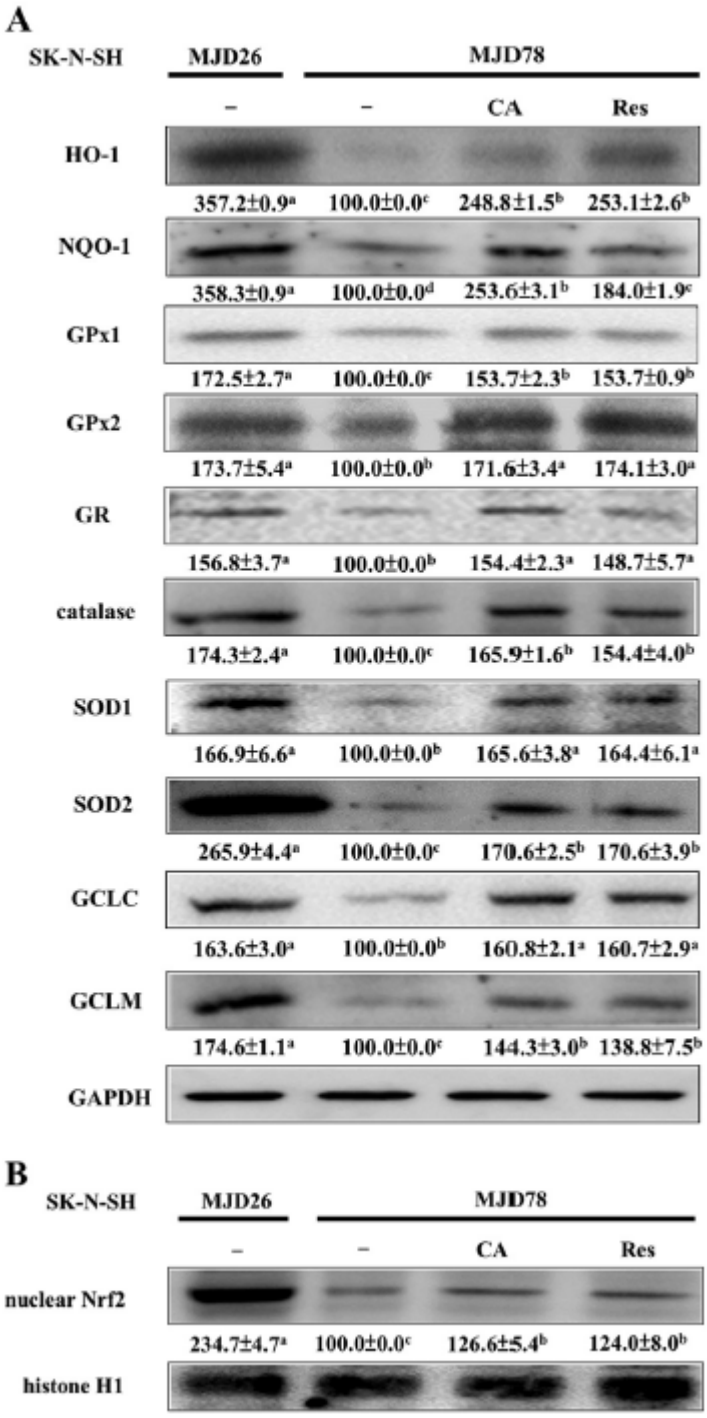


Table 2
Effects of CA and Res on ROS and GSH levels in SK-N-SH-MJD78 cells*.

SK-N-SH	WT	MJD26	MJD78		
	DMSO	DMSO	DMSO	CA	Res
H_2DCFDA#	8.1 ± 0.2^c	11.5 ± 0.8^c	100.0 ± 0.0^a	30.2 ± 1.3^b	31.7 ± 1.1^b
MitoSOX#	12.6 ± 0.5^c	12.6 ± 1.0^c	100.0 ± 0.0^a	31.2 ± 3.3^b	30.3 ± 3.3^b
GSH#	NT	333.8 ± 3.2^a	100.0 ± 0.0^c	235.1 ± 3.1^b	232.4 ± 3.0^b

* Cells were treated with or without DMSO vehicle control or 3 μM CA or Res for 24 h except for measurement of H_2DCFDA (18 h treatment).
# Values are expressed as the percentage of SK-N-SH-MJD78 cells treated with the vehicle control. Data are means ± SD of at least three separate experiments and not sharing the same



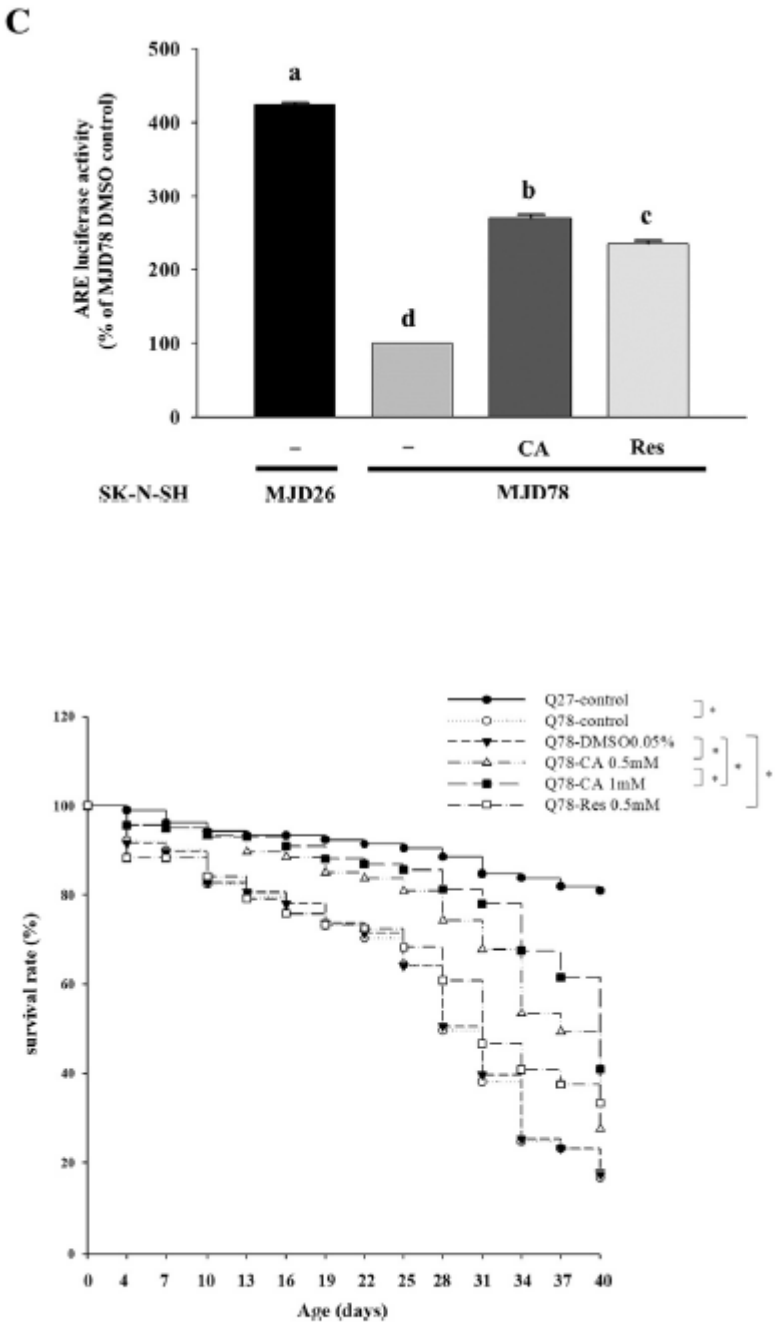
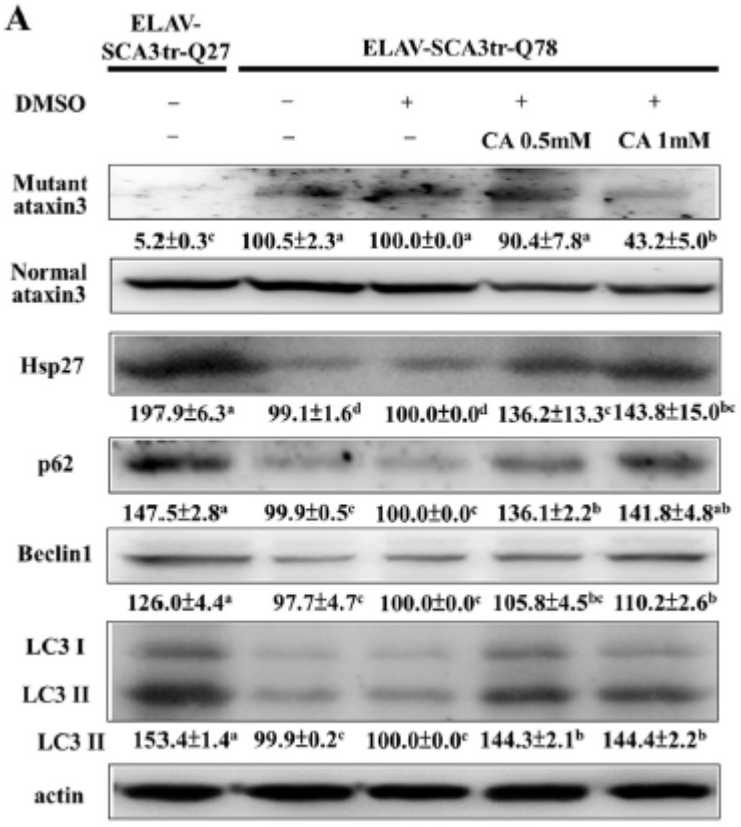


Fig. 5. Effects of CA and Res on survival in ELAV-SCA3tr-Q78 transgenic *Drosophila*. Survival rates were compared across groups by Kaplan-Meier log rank analysis. The mean life-span and SD are shown, * $P < 0.01$ (n = 320).


A
ELAV-SCA3tr-Q27
ELAV-SCA3tr-Q78
DMSO
CA 0.5mM
CA 1mM
Mutant ataxin3
5.2±0.3c 100.5±2.3a 100.0±0.0a 90.4±7.8a 43.2±5.0b
Normal ataxin3
Hsp27
197.9±6.3a 99.1±1.6d 100.0±0.0d 136.2±13.3c 143.8±15.0bc
p62
147.5±2.8a 99.9±0.5c 100.0±0.0c 136.1±2.2b 141.8±4.8ab
Beclin1
126.0±4.4a 97.7±4.7c 100.0±0.0c 105.8±4.5bc 110.2±2.6b
LC3 I
LC3 II
LC3 II 153.4±1.4a 99.9±0.2c 100.0±0.0c 144.3±2.1b 144.4±2.2b
actin

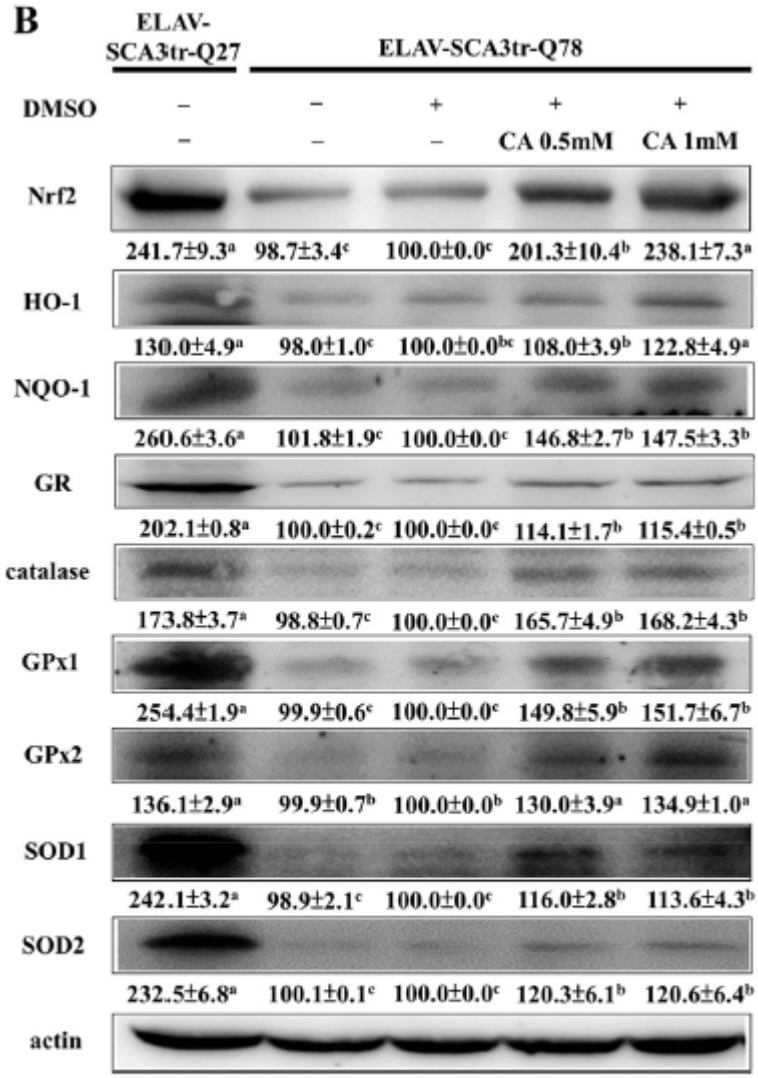


Fig. 6. Effects of CA on ELAV-SCA3tr-Q78 transgenic *Drosophila*. In 19-day-old female ELAV-SCA3tr-Q78 flies, (A) and (B) protein expression of mutant and normal ataxin-3, Hsp27, p62, Beclin-1, LC3-II, Nrf2, HO-1, NQO1, GPx, GR, catalase, and SOD. Values are means ± SD, n = 30 female flies in three separate experiments. The values are expressed as the percentage of ELAV-SCA3tr-Q78 flies treated with the vehicle control. In ELAV-SCA3tr-Q78 fly groups, values not sharing the same letter are significantly different ($P < 0.05$).

106年度專題研究計畫成果彙整表

計畫主持人：劉凱莉	**計畫編號：**106-2320-B-040-025-MY3
計畫名稱：以細胞、果蠅及動物模式探討咖啡酸改善第三型脊髓小腦運動失調症神經細胞凋亡及氧化壓力的功效及相關機制	

成果項目			量化	單位	質化 （說明：各成果項目請附佐證資料或細項說明，如期刊名稱、年份、卷期、起訖頁數、證號...等）
國內	學術性論文	期刊論文	0	篇	
		研討會論文	1		2016AOMC, Caffeic acid and resveratrol through increasing Nrf2 transcriptional activity and autophagy activaiton prevent protein aggregation and oxidative stress in human neuroblastoma stable transfected with mutant ataxin-3 , Yu-Ling Wu1, Whei-Ling Chiang2, Chin-San Liu3, Kai-Li Liu1
		專書	0	本	
		專書論文	1	章	Effects of Caffeic Acid and Resveratrol on Oxidative Stress induced neurotoxicity in Cell and Drosophila Models of Spinocerebellar Ataxia Type3 咖啡酸和白藜蘆醇對改善氧化壓力誘發第三型脊髓小腦運動失調症細胞與果蠅模式的神經毒性之功效 巫玉琳
		技術報告	0	篇	
		其他	0	篇	
國外	學術性論文	期刊論文	2	篇	Wu YL, Chang JC, Lin WY, Li CC, Hsieh M, Chen HW, Wang TS, Wu WT, Liu CS, Liu KL (通訊作者). Caffeic acid and resveratrol ameliorate cellular damage in cell and Drosophila models of spinocerebellar ataxia type 3 through upregulation of Nrf2 pathway. Free Radic Biol Med. 2018 Feb 1;115:309-317. Wu YL, Chang JC, Lin WY, Li CC, Hsieh M, Chen HW, Wang TS, Liu CS, Liu KL (通訊作者). Treatment with Caffeic Acid and Resveratrol Alleviates Oxidative Stress Induced Neurotoxicity in Cell and Drosophila Models of

					Spinocerebellar Ataxia Type3. Sci Rep. 2017 Sep 14;7(1):11641
		研討會論文	0		
		專書	0	本	
		專書論文	0	章	
		技術報告	0	篇	
		其他	0	篇	
參與計畫人力	本國籍	大專生	0	人次	
		碩士生	6		林哲群，吳宜靜, 施采瑩, 呂雅珍， 林雅婷， 廖弈婷
		博士生	1		巫玉琳
		博士級研究人員	0		
		專任人員	2		顏玉珮，張雅雯
	非本國籍	大專生	0		
		碩士生	0		
		博士生	0		
		博士級研究人員	0		
		專任人員	0		
其他成果 （無法以量化表達之成果如辦理學術活動、獲得獎項、重要國際合作、研究成果國際影響力及其他協助產業技術發展之具體效益事項等，請以文字敘述填列。）					