Supplementary material

## Flutamide induces uterus and ovary damage in the mouse via apoptosis and excessive autophagy of cells following triggering of the unfolded protein response

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genes		uterus		ovary	
		control	flutamide	control	
Grp78	5.85±1.52*	$1.00{\pm}0.01$	$7.93{\pm}0.78^{*}$	$1.00{\pm}0.01$	
Perk	$18.90{\pm}3.76^*$	$1.00{\pm}0.01$	33.93±6.46*	$1.00{\pm}0.01$	
Irel	92.06±19.1*	$1.00{\pm}0.01$	11.22±3.12*	$1.00{\pm}0.01$	
Atf6	31.64±4.95*	$1.00{\pm}0.01$	34.69±6.17*	$1.00{\pm}0.01$	
eIF2a	4.73±1.26*	$1.00{\pm}0.01$	$1.09{\pm}0.41$	$1.00{\pm}0.01$	
Atf4	9.20±3.68*	$1.00{\pm}0.01$	$4.94{\pm}1.14^{*}$	$1.00{\pm}0.01$	
Xbp1	15.46±2.97*	$1.00{\pm}0.01$	7.06±1.33*	$1.00{\pm}0.01$	
Chop	16.38±2.54*	$1.00{\pm}0.01$	3.24±1.23*	$1.00{\pm}0.01$	
Ulk1	2.06±0.21*	1.00±0.01	0.17±0.06 <sup>#</sup>	$1.00{\pm}0.01$	
Atg3	30.06±5.94*	$1.00{\pm}0.01$	$4.83{\pm}0.97^{*}$	$1.00{\pm}0.01$	
Lc3b	39.15±4.72*	$1.00{\pm}0.01$	0.04±0.01 <sup>#</sup>	$1.00{\pm}0.01$	
Beclinl	1.84±0.29*	$1.00{\pm}0.01$	1.08±0.37	$1.00{\pm}0.01$	
Atg7	15.30±2.46*	$1.00 \pm 0.01$	3.15±0.83*	$1.00 \pm 0.01$	
Askl	10 70+2 01*	1 00+0 01	11 90+3 32*	1 00+0 01	
Aktl	$16.76\pm 3.20^{*}$	$1.00\pm0.01$	$5.30 \pm 1.26^*$	$1.00\pm0.01$ 1.00+0.01	
Nf-rh	$10.70\pm3.27$ $12.02\pm3.60^*$	$1.00\pm0.01$	5.50±1.20	$1.00\pm0.01$ 1.00±0.01	
Traf?	$12.02\pm3.00$ 1.62+0.26*	$1.00\pm0.01$	0.05±0.90 1 96±0 39*	$1.00\pm0.01$ 1.00+0.01	
Inkl	$1.02\pm0.20$ 23.86±7.75*	$1.00\pm0.01$	$1.90\pm0.57$ 1.28±0.57	$1.00\pm0.01$ 1.00+0.01	
Jnk?	$19,00+4,20^*$	$1.00\pm0.01$ 1.00+0.01	$1.28\pm0.37$ 1.08+0.34	$1.00\pm0.01$ 1.00+0.01	
Ink3	$13.00 \pm 4.20$ 23.87+3.50*	$1.00\pm0.01$	$1.00\pm0.34$ 1 10+0 31	$1.00\pm0.01$ 1.00+0.01	
Caspase 3	$23.87\pm3.50$ $22.20+3.43^*$	$1.00\pm0.01$	$7.85+0.85^*$	$1.00\pm0.01$ $1.00\pm0.01$	
Caspase 9	$47 82+4 63^*$	1 00+0 01	15 12+2 86*	1 00+0 01	
Caspase 12	$9.80 \pm 1.33^*$	$1.00\pm0.01$	$25.60+4.12^*$	$1.00\pm0.01$	
Bcl-xl	8.69±1.78*	$1.00 \pm 0.01$	12.62±2.87*	$1.00\pm0.01$	
Conal	1 10+0 45	1 00+0 01	0 07±0 12	1 00+0 01	
Cenhl	$1.19\pm0.43$ 0.92±0.17	$1.00\pm0.01$ 1.00+0.01	$0.9/\pm0.13$ 0.81±0.41	$1.00\pm0.01$ 1.00±0.01	
Cono	0.92±0.17	$1.00\pm0.01$ 1.00±0.01	$0.01\pm0.41$	$1.00\pm0.01$ 1.00±0.01	
Cendl	1.14±0.49 1.02⊥0.22	$1.00\pm0.01$ 1.00+0.01	$0.92\pm0.27$ 0.85±0.27	1.00±0.01 1.00±0.01	
Conal	1.02±0.23	$1.00\pm0.01$ 1.00±0.01	$0.03\pm0.32$	$1.00\pm0.01$ 1.00±0.01	
CD44	$1.1/\pm0.40$	$1.00\pm0.01$ 1.00±0.01	$0.03\pm0.31$	$1.00\pm0.01$ 1.00±0.01	
	nes Grp 78 Perk Ire 1 Atf6 eIF 2a Atf4 Xbp 1 Chop Ulk1 Atg3 Lc3b Beclinl Atg7 Ask1 Atg7 Ask1 Akt1 Nf-kb Traf2 Jnk1 Jnk2 Jnk3 Caspase 3 Caspase 3 Caspase 12 Bcl-xl Ccna 1 Ccnb 1 Ccnc Ccnd 1 Ccne 1 CD44	nesutenfluta mideGrp 78 $5.85\pm 1.52^*$ Perk $18.90\pm 3.76^*$ Ire I $92.06\pm 19.1^*$ Atf6 $31.64\pm 4.95^*$ elF2a $4.73\pm 1.26^*$ Atf4 $9.20\pm 3.68^*$ Xbp1 $15.46\pm 2.97^*$ Chop $16.38\pm 2.54^*$ Ulk1 $2.06\pm 0.21^*$ Atg3 $30.06\pm 5.94^*$ Lc3b $39.15\pm 4.72^*$ Beclinl $1.84\pm 0.29^*$ Atg7 $15.30\pm 2.46^*$ Ask1 $10.70\pm 2.01^*$ Akt1 $16.76\pm 3.29^*$ Nf-kb $12.02\pm 3.60^*$ Traf2 $1.62\pm 0.26^*$ Jnk1 $23.86\pm 7.75^*$ Jnk2 $19.00\pm 4.20^*$ Jnk3 $23.87\pm 3.50^*$ Caspase 3 $22.20\pm 3.43^*$ Caspase 4 $7.82\pm 4.63^*$ Caspase 12 $9.80\pm 1.33^*$ Bcl-xl $8.69\pm 1.78^*$ Ccnal $1.19\pm 0.45$ Ccncl $1.14\pm 0.49$ Ccnd1 $1.02\pm 0.23$ Ccnel $1.17\pm 0.48$ CD44 $1.04\pm 0.34$	uterusfluta midecontrolGrp 78 $5.85\pm 1.52^*$ $1.00\pm 0.01$ Perk $18.90\pm 3.76^*$ $1.00\pm 0.01$ Irel $92.06\pm 19.1^*$ $1.00\pm 0.01$ Att6 $31.64\pm 4.95^*$ $1.00\pm 0.01$ Att6 $31.64\pm 4.95^*$ $1.00\pm 0.01$ Att74 $9.20\pm 3.68^*$ $1.00\pm 0.01$ Chop $16.38\pm 2.54^*$ $1.00\pm 0.01$ Chop $16.38\pm 2.54^*$ $1.00\pm 0.01$ Attg3 $30.06\pm 5.94^*$ $1.00\pm 0.01$ Attg3 $30.06\pm 5.94^*$ $1.00\pm 0.01$ Attg7 $15.30\pm 2.46^*$ $1.00\pm 0.01$ Attg7 $15.30\pm 2.46^*$ $1.00\pm 0.01$ Attg7 $1.62\pm 0.26^*$ $1.00\pm 0.01$ Mt1 $16.76\pm 3.29^*$ $1.00\pm 0.01$ Mt2 $19.00\pm 4.20^*$ $1.00\pm 0.01$ Jnk1 $23.86\pm 7.75^*$ $1.00\pm 0.01$ Jnk2 $19.00\pm 4.20^*$ $1.00\pm 0.01$ Jnk3 $23.87\pm 3.50^*$ $1.00\pm 0.01$ Caspase 3 $22.20\pm 3.43^*$ $1.00\pm 0.01$ Caspase 12 $9.80\pm 1.33^*$ $1.00\pm 0.01$ Ccna1 $1.19\pm 0.45$ $1.00\pm 0.01$ Ccna1 $1.02\pm 0.23$ $1.00\pm 0.01$ Ccna1	uterus         ova $Grp78$ $5.85\pm 1.52^*$ $1.00\pm 0.01$ $7.93\pm 0.78^*$ $Perk$ $18.90\pm 3.76^*$ $1.00\pm 0.01$ $33.93\pm 6.46^*$ $Irel$ $92.06\pm 19.1^*$ $1.00\pm 0.01$ $31.93\pm 6.46^*$ $Irel$ $92.06\pm 19.1^*$ $1.00\pm 0.01$ $31.69\pm 6.17^*$ $Atf6$ $31.64\pm 4.95^*$ $1.00\pm 0.01$ $34.69\pm 6.17^*$ $elF2a$ $4.73\pm 1.26^*$ $1.00\pm 0.01$ $4.94\pm 1.14^*$ $Xbp1$ $15.46\pm 2.97^*$ $1.00\pm 0.01$ $4.94\pm 1.14^*$ $Xbp1$ $15.46\pm 2.97^*$ $1.00\pm 0.01$ $7.06\pm 1.33^*$ $Chop$ $16.38\pm 2.54^*$ $1.00\pm 0.01$ $0.17\pm 0.06^{\#}$ $Atg3$ $30.06\pm 5.94^*$ $1.00\pm 0.01$ $0.04\pm 0.01^{\#}$ $Beclinl$ $1.84\pm 0.29^*$ $1.00\pm 0.01$ $1.08\pm 0.37$ $Atg7$ $15.30\pm 2.46^*$ $1.00\pm 0.01$ $1.90\pm 3.32^*$ $Akt1$ $16.76\pm 3.29^*$ $1.00\pm 0.01$ $1.96\pm 0.39^*$ $Jnk2$ $12.02\pm 3.60^*$ $1.00\pm 0.01$ $1.28\pm 0.57$ $Jnk2$	

Table S1The mRNA abundance of all the genes were measured (n=12)

Note: \*: higher than the control group, #: lower than the control, P<0.05, t test, n=12

The abundance of the OPR-felated key proteins and CCho1 (h=0)						
proteins –	uterus		ovary			
	flutamide	control	flutamide	control		
Perk	$1.070297 \pm$	$0.706044\pm$	$1.067731\pm$	$0.82905 \pm$		
	0.133136*	0.190418	0.150577*	0.132117795		
p-EIf2a	$0.255345 \pm$	0	$0.297297 \pm$	0		
	0.051452*	0	0.073599*	0		
Atf6	$0.471336 \pm$	0.361516±	$0.570475 \pm$	$0.442125\pm$		
	0.0619*	0.031634	0.061542*	0.086697461		
Grp78	$0.804789 \pm$	$0.573772 \pm$	$0.559758 \pm$	$0.299572 \pm$		
	0.110131*	0.026138	0.072363*	0.053155946		
Ire1	$0.1735823 \pm$	$0.111266 \pm$	0.232176±	$0.084285 \pm$		
	0.028942*	0.04433	0.057233*	0.021057305		
Cenb1	$0.869870484 \pm$	$0.825871 \pm$	$1.244989 \pm$	$1.22413 \pm$		
	0.134541	0.091588	0.211691	0.216849964		

**Table S2** The abundance of the UPR-related key proteins and CCnb1 (n=6)

Note: \*: higher than the control group, *P*<0.05, t test, n=6