

DEVELOPMENTAL NEUROTOXICITY OF ORGANOPHOSPHATES

TARGETS CELL CYCLE AND APOPTOSIS, REVEALED BY

TRANSCRIPTIONAL PROFILES IN VIVO AND IN VITRO

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SUPPLEMENTAL TABLES

Supplemental Table 1 (continued)									
<i>stag3</i>	1.10 ± 0.04	0.85 ± 0.06		1.16 ± 0.12	0.86 ± 0.06		1.07 ± 0.08	0.87 ± 0.06	
<i>stk6</i>	0.96 ± 0.03	1.21 ± 0.09	*	0.80 ± 0.04	1.02 ± 0.05		0.88 ± 0.10	1.08 ± 0.05	
<i>tacc1a</i>	0.99 ± 0.03	0.95 ± 0.05		1.05 ± 0.03	0.96 ± 0.03		1.04 ± 0.04	1.00 ± 0.03	
<i>tcf19</i>	0.85 ± 0.03	1.09 ± 0.05		0.87 ± 0.02	1.14 ± 0.03		0.87 ± 0.01	1.13 ± 0.02	
<i>tgfa</i>	1.00 ± 0.03	1.07 ± 0.04		0.97 ± 0.02	1.06 ± 0.02		1.04 ± 0.06	1.03 ± 0.02	*
<i>tgbf1</i>	0.99 ± 0.05	1.01 ± 0.05	*	1.16 ± 0.06	1.05 ± 0.05		0.99 ± 0.05	0.96 ± 0.05	
<i>tgbf2</i>	0.87 ± 0.02	1.30 ± 0.07		0.88 ± 0.05	1.37 ± 0.05		0.89 ± 0.04	1.18 ± 0.05	
<i>tgbf3</i>	0.77 ± 0.06	1.32 ± 0.13		0.85 ± 0.06	1.20 ± 0.06	†	0.90 ± 0.04	1.10 ± 0.05	
<i>thpo</i>	0.87 ± 0.08	0.97 ± 0.05		0.94 ± 0.04	1.02 ± 0.03		0.86 ± 0.08	1.04 ± 0.05	*
<i>thra</i>	0.64 ± 0.03	1.91 ± 0.17	†	0.65 ± 0.04	1.52 ± 0.04†	†	0.66 ± 0.02	1.52 ± 0.06†	†
<i>tp53</i>	0.93 ± 0.03	1.20 ± 0.04	*†	0.93 ± 0.02	1.03 ± 0.03†	*†	0.99 ± 0.03	0.97 ± 0.01†	†
<i>trp63</i>	0.83 ± 0.09	1.05 ± 0.10		1.02 ± 0.06	0.96 ± 0.09	†	1.06 ± 0.07	0.92 ± 0.05	†
<i>tsc1</i>	0.88 ± 0.08	1.01 ± 0.06		1.00 ± 0.10	1.10 ± 0.05		0.97 ± 0.09	0.92 ± 0.06	
<i>tsc2</i>	0.87 ± 0.01	1.18 ± 0.09		0.87 ± 0.04	1.04 ± 0.04		0.89 ± 0.05	1.07 ± 0.02	
<i>ube1c</i>	0.99 ± 0.03	0.97 ± 0.05		0.97 ± 0.03	1.04 ± 0.01		0.99 ± 0.01	1.04 ± 0.01	
<i>uchl1</i>	0.94 ± 0.05	1.03 ± 0.09		1.04 ± 0.04	0.98 ± 0.05		1.03 ± 0.03	1.00 ± 0.05	
<i>uchl3</i>	1.12 ± 0.02	0.88 ± 0.02		1.14 ± 0.03	0.90 ± 0.02		1.13 ± 0.03	0.91 ± 0.02	
<i>vav1</i>	0.92 ± 0.11	0.98 ± 0.16		1.03 ± 0.08	1.01 ± 0.14		1.16 ± 0.16	1.11 ± 0.15	
<i>vegf</i>	0.95 ± 0.03	1.02 ± 0.02		0.93 ± 0.02	1.04 ± 0.02		0.95 ± 0.02	1.04 ± 0.02	
<i>vegfb</i>	1.23 ± 0.03	1.03 ± 0.06	*	1.09 ± 0.02	0.93 ± 0.02	*	1.12 ± 0.04	0.92 ± 0.03	*
<i>vegfc</i>	1.00 ± 0.02	1.13 ± 0.04		0.96 ± 0.02	1.07 ± 0.03	*	0.96 ± 0.02	1.02 ± 0.02	*†
<i>vhl</i>	1.04 ± 0.02	1.00 ± 0.02		1.04 ± 0.02	0.98 ± 0.01		1.02 ± 0.04	0.96 ± 0.02	
<i>wt1</i>	0.86 ± 0.13	0.81 ± 0.17	*	1.05 ± 0.17	1.60 ± 0.07		0.87 ± 0.11	0.88 ± 0.11	*†
									0.92 ± 0.07
									1.46 ± 0.11†

Normalized expression ratios are given as mean ± SE obtained from five animals in each group, with the sample from each animal run on a separate array. CPF1 = 1 mg/kg chlorpyrifos; DZN1 = 1 mg/kg diazinon; DZN2 = 2 mg/kg diazinon. Several of the values reported in this table have appeared in previous studies of other gene groupings [2,7-9].

*Significant main treatment effect in two-factor ANOVA (treatment, region).

†Interaction of treatment × region; then, † denotes significant treatment effect for a given region.

Global statistical analysis of Table 1: ANOVA factors of treatment, gene, region[§]

All treatments: treatment × gene p < 0.0001; treatment × gene × region, p < 0.0001

brainstem: treatment × gene, p < 0.0001

forebrain: treatment × gene, p < 0.0001

Control vs. CPF1: treatment × gene, p < 0.0001; treatment × gene × region, p < 0.002

brainstem: treatment × gene, p < 0.001

forebrain: treatment × gene, p < 0.0001

Control vs. DZN1: treatment × gene, p < 0.0001; treatment × gene × region, p < 0.002

brainstem: treatment × gene, p < 0.0001

forebrain: treatment × gene, p < 0.0001

Control vs. DZN2: treatment × gene, p < 0.0001; treatment × gene × region, p < 0.0001

brainstem: treatment × gene, p < 0.0004

forebrain: treatment × gene, p < 0.0001

[§]results shown include only treatment effects and interactions of treatment with other variables

Supplemental Table 2 (continued)

<i>rtn4</i>	0.87 ± 0.03	1.09 ± 0.06		0.93 ± 0.04	1.08 ± 0.03		0.99 ± 0.06	1.11 ± 0.05	
<i>s100b</i>	1.59 ± 0.14	0.85 ± 0.07		1.49 ± 0.20	0.69 ± 0.13		1.49 ± 0.20	0.66 ± 0.14	
<i>scn2a1</i>	0.95 ± 0.04	1.00 ± 0.04		0.95 ± 0.03	1.03 ± 0.03		0.97 ± 0.03	1.05 ± 0.03	
<i>sgk</i>	0.94 ± 0.04	1.24 ± 0.07		0.87 ± 0.04	1.17 ± 0.06	*	0.87 ± 0.04	1.11 ± 0.05	
<i>sh3kbp1</i>	0.99 ± 0.02	0.98 ± 0.04		0.98 ± 0.02	1.00 ± 0.02		1.03 ± 0.04	1.02 ± 0.01	
<i>sh3md2</i>	1.01 ± 0.09	1.10 ± 0.05		0.97 ± 0.14	0.98 ± 0.08		1.01 ± 0.09	1.02 ± 0.07	†
<i>siah2</i>	0.89 ± 0.05	1.12 ± 0.06		0.86 ± 0.07	1.01 ± 0.01		0.98 ± 0.06	1.04 ± 0.02	
<i>sod1</i>	1.29 ± 0.03	0.69 ± 0.02	*	1.42 ± 0.02	0.72 ± 0.01	*	1.47 ± 0.03	0.74 ± 0.02	*
<i>spata3</i>	1.15 ± 0.08	0.89 ± 0.05	†	1.03 ± 0.06	1.02 ± 0.03†	†	1.05 ± 0.09	1.09 ± 0.05†	†
<i>spp1</i>	1.67 ± 0.09	0.62 ± 0.07		1.73 ± 0.19	0.57 ± 0.09		1.59 ± 0.12	0.52 ± 0.06	
<i>stambp</i>	1.00 ± 0.01	1.13 ± 0.01	*	0.94 ± 0.01	1.06 ± 0.01	*†	0.95 ± 0.01†	0.97 ± 0.02†	*†
<i>stk17b</i>	0.97 ± 0.04	1.06 ± 0.05		0.96 ± 0.03	1.03 ± 0.04		0.97 ± 0.06	1.01 ± 0.01	
<i>stk3</i>	1.09 ± 0.07	0.95 ± 0.02		1.17 ± 0.04	0.94 ± 0.02		1.09 ± 0.06	0.92 ± 0.01	
<i>stnl</i>	1.05 ± 0.04	0.98 ± 0.06		1.14 ± 0.04	0.93 ± 0.03	†	1.19 ± 0.04†	0.89 ± 0.02	
<i>tax1bp1</i>	1.00 ± 0.02	0.99 ± 0.01		0.99 ± 0.01	0.99 ± 0.02		1.02 ± 0.02	1.00 ± 0.02	
<i>tegt</i>	1.02 ± 0.04	1.07 ± 0.02		0.96 ± 0.03	1.05 ± 0.03	*	0.94 ± 0.02	1.03 ± 0.01	*
<i>tesk2</i>	1.01 ± 0.09	0.92 ± 0.07		1.12 ± 0.10	1.05 ± 0.09		0.98 ± 0.04	0.92 ± 0.11	
<i>tfpt</i>	0.92 ± 0.04	1.07 ± 0.06		0.90 ± 0.07	1.09 ± 0.08		0.98 ± 0.05	0.99 ± 0.04	
<i>tgfa</i>	1.00 ± 0.03	1.07 ± 0.04		0.97 ± 0.02	1.06 ± 0.02		1.04 ± 0.06	1.03 ± 0.02	
<i>tgm2</i>	0.98 ± 0.05	1.14 ± 0.03		0.90 ± 0.05	1.07 ± 0.04	*	0.88 ± 0.03	1.02 ± 0.03	
<i>thap1</i>	0.87 ± 0.06	0.93 ± 0.07		0.87 ± 0.09	1.04 ± 0.08	*	1.12 ± 0.14	1.15 ± 0.17	
<i>tieg</i>	1.08 ± 0.05	1.10 ± 0.02	*	1.01 ± 0.04	1.03 ± 0.02	*	0.97 ± 0.02	0.99 ± 0.02	*
<i> timp3</i>	0.95 ± 0.06	0.97 ± 0.10		1.13 ± 0.10	1.06 ± 0.13		0.99 ± 0.05	0.99 ± 0.09	
<i>tnf</i>	1.75 ± 0.26	0.89 ± 0.12	†	0.99 ± 0.11†	1.11 ± 0.13	†	1.29 ± 0.18†	1.04 ± 0.09	*†
<i>tnfrsf11b</i>	1.04 ± 0.07	0.85 ± 0.04	*	1.15 ± 0.07	0.98 ± 0.03		1.04 ± 0.04	0.96 ± 0.03	*
<i>tnfrsf1a</i>	1.24 ± 0.01	0.97 ± 0.02	*	1.16 ± 0.05	0.95 ± 0.01	*	1.15 ± 0.05	0.94 ± 0.02	*
<i>tnfrsf6</i>	1.10 ± 0.09	0.94 ± 0.18	*	1.39 ± 0.05	1.01 ± 0.05		1.18 ± 0.10	0.84 ± 0.04	
<i>tnfsf10</i>	1.48 ± 0.32	0.90 ± 0.20		1.20 ± 0.25	0.96 ± 0.15		1.00 ± 0.21	1.30 ± 0.32	
<i>tp53</i>	0.93 ± 0.03	1.20 ± 0.04	*†	0.93 ± 0.02	1.03 ± 0.03†	*†	0.99 ± 0.03	0.97 ± 0.01†	†
<i>tpt1</i>	1.04 ± 0.04	1.04 ± 0.02	*	0.95 ± 0.01	0.97 ± 0.04		0.97 ± 0.02	1.01 ± 0.03	
<i>tradd</i>	1.24 ± 0.06	0.89 ± 0.08		1.23 ± 0.06	0.93 ± 0.04		1.14 ± 0.06	0.83 ± 0.03	
<i>trib3</i>	1.21 ± 0.03	0.83 ± 0.03		1.29 ± 0.03	0.82 ± 0.04	*	1.36 ± 0.04	0.85 ± 0.02	
<i>trp63</i>	0.83 ± 0.09	1.05 ± 0.10		1.02 ± 0.06	0.96 ± 0.09	†	1.06 ± 0.07	0.92 ± 0.05	†
<i>tsarg1</i>	1.10 ± 0.09	0.97 ± 0.05		0.99 ± 0.08	1.04 ± 0.07		1.00 ± 0.12	0.99 ± 0.09	
<i>twist2</i>	1.03 ± 0.06	0.81 ± 0.06	†	0.92 ± 0.05	1.13 ± 0.08†	†	0.92 ± 0.04	0.99 ± 0.07†	*
<i>txnl1</i>	1.00 ± 0.01	0.97 ± 0.02		0.97 ± 0.02	0.97 ± 0.02		1.00 ± 0.02	0.99 ± 0.02	
<i>ube1c</i>	0.99 ± 0.03	0.97 ± 0.05		0.97 ± 0.03	1.04 ± 0.01		0.99 ± 0.01	1.04 ± 0.01	
<i>unc5a</i>	0.97 ± 0.06	1.03 ± 0.02		1.03 ± 0.05	0.99 ± 0.04		0.94 ± 0.07	1.07 ± 0.04	
<i>unc5b</i>	1.04 ± 0.10	1.12 ± 0.17		0.90 ± 0.07	1.04 ± 0.08		0.98 ± 0.04	1.00 ± 0.08	
<i>v1rd22</i>	1.07 ± 0.11	1.09 ± 0.05		1.00 ± 0.07	1.00 ± 0.03		0.96 ± 0.07	1.08 ± 0.05	
<i>vdr</i>	0.92 ± 0.08	0.84 ± 0.05	*	1.30 ± 0.11	1.06 ± 0.06	†	1.32 ± 0.07†	0.81 ± 0.09	†
<i>vegf</i>	0.95 ± 0.03	1.02 ± 0.02		0.93 ± 0.02	1.04 ± 0.02		0.95 ± 0.02	1.04 ± 0.02	
<i>wig1</i>	1.08 ± 0.02	0.92 ± 0.02		1.02 ± 0.03	0.92 ± 0.04		1.10 ± 0.01	0.96 ± 0.02	
<i>ywhah</i>	0.98 ± 0.03	1.00 ± 0.03		1.02 ± 0.01	0.99 ± 0.02		1.03 ± 0.01	0.97 ± 0.02	
<i>zd10b</i>	0.94 ± 0.04	1.08 ± 0.04		0.90 ± 0.03	1.08 ± 0.04		0.89 ± 0.02	1.09 ± 0.04	
<i>zfp162</i>	0.98 ± 0.18	1.45 ± 0.13	*	0.74 ± 0.03	1.05 ± 0.11		1.07 ± 0.07	1.17 ± 0.12	
									0.90 ± 0.06
									1.08 ± 0.04

Normalized expression ratios are given as mean ± SE obtained from five animals in each group, with the sample from each animal run on a separate array. CPF1 = 1 mg/kg chlorpyrifos; DZN1 = 1 mg/kg diazinon; DZN2 = 2 mg/kg diazinon. Several of the values reported in this table have appeared in previous studies of other gene groupings [2,7-9].

*Significant main treatment effect in two-factor ANOVA (treatment, region).

†Interaction of treatment × region; then, † denotes significant treatment effect for a given region.

Global statistical analysis of Table 2: ANOVA factors of treatment, gene, region[§]

All treatments: treatment main effect, p < 0.0009; treatment × gene p < 0.0001; treatment × gene × region, p < 0.0007

brainstem: treatment × gene, p < 0.0001

forebrain: treatment main effect, p < 0.008; treatment × gene, p < 0.0001

Control vs. CPF1: treatment main effect (Control > CPF1), p < 0.05; treatment × gene, p < 0.0001; treatment × gene × region, p < 0.0003

brainstem: treatment × gene, p < 0.03

forebrain: treatment × gene, p < 0.0001

Control vs. DZN1: treatment main effect (Control > DZN1), p < 0.02; treatment × gene, p < 0.0001; treatment × gene × region, p < 0.0001

brainstem: treatment × gene, p < 0.0001

forebrain: treatment main effect (Control > DZN1), p < 0.05; treatment × gene, p < 0.0005

Control vs. DZN2: main effect of treatment (Control > DZN2), p < 0.0001; treatment × gene, p < 0.0001; treatment × gene × region, p < 0.0001

brainstem: treatment main effect (Control > DZN2), p < 0.02; treatment × gene, p < 0.0001

forebrain: treatment main effect (Control > DZN2), p < 0.002; treatment × gene, p < 0.0001

[§]results shown include only treatment effects and interactions of treatment with other variables

Supplemental Table 3 (continued)

<i>stag3</i>	0.84 ± 0.16	1.07 ± 0.15		0.94 ± 0.16	1.11 ± 0.12	0.92 ± 0.11	1.02 ± 0.07	*	1.22 ± 0.13	1.14 ± 0.13
<i>stk6</i>	0.99 ± 0.03	1.11 ± 0.01		1.02 ± 0.01	1.16 ± 0.02	0.95 ± 0.04	0.88 ± 0.04	*	0.91 ± 0.02	0.79 ± 0.03
<i>tacc1a</i>	1.07 ± 0.04	1.04 ± 0.07		1.01 ± 0.05	1.02 ± 0.06	1.03 ± 0.05	0.99 ± 0.04		1.06 ± 0.05	0.91 ± 0.06
<i>tcf19</i>	1.14 ± 0.02	1.07 ± 0.02	*	1.12 ± 0.01	1.01 ± 0.01	0.96 ± 0.02	0.76 ± 0.02	*	0.92 ± 0.01	0.69 ± 0.01
<i>tgfa</i>	1.20 ± 0.06	1.16 ± 0.10	*	0.98 ± 0.07	0.96 ± 0.05	1.07 ± 0.08	0.85 ± 0.03	†	0.96 ± 0.04	1.28 ± 0.17†
<i>tgfb1</i>	0.84 ± 0.08	1.11 ± 0.12		0.78 ± 0.10	1.06 ± 0.06	1.58 ± 0.28	1.22 ± 0.18	**†	0.89 ± 0.11†	1.08 ± 0.07
<i>tgfb2</i>	1.18 ± 0.24	1.07 ± 0.17		1.23 ± 0.33	0.92 ± 0.18	0.65 ± 0.17	1.35 ± 0.17	†	1.00 ± 0.12	0.91 ± 0.12
<i>tgfb3</i>	1.00 ± 0.05	1.05 ± 0.08		0.94 ± 0.04	0.94 ± 0.04	1.17 ± 0.09	1.02 ± 0.04	†	0.95 ± 0.04	1.18 ± 0.09
<i>thpo</i>	0.89 ± 0.09	0.95 ± 0.09		1.06 ± 0.11	1.03 ± 0.03	0.88 ± 0.08	1.01 ± 0.07		1.05 ± 0.07	0.99 ± 0.04
<i>thra</i>	1.10 ± 0.02	1.19 ± 0.03		1.08 ± 0.05	1.08 ± 0.05	0.90 ± 0.04	0.89 ± 0.04		0.84 ± 0.03	0.85 ± 0.01
<i>tp53</i>	1.38 ± 0.16	1.41 ± 0.19	*	1.04 ± 0.06	1.10 ± 0.08	0.95 ± 0.10	0.90 ± 0.11		0.93 ± 0.03	0.69 ± 0.04
<i>trp63</i>	1.07 ± 0.17	1.11 ± 0.20		0.88 ± 0.14	0.92 ± 0.13	1.12 ± 0.18	0.96 ± 0.05		1.00 ± 0.05	0.90 ± 0.12
<i>tsc1</i>	0.90 ± 0.03	1.13 ± 0.04		0.89 ± 0.05	1.00 ± 0.10	1.07 ± 0.12	1.05 ± 0.11		1.07 ± 0.08	1.06 ± 0.05
<i>tsc2</i>	1.00 ± 0.03	1.06 ± 0.04		0.97 ± 0.02	1.10 ± 0.03	0.99 ± 0.02	0.98 ± 0.03	**†	1.11 ± 0.02†	0.98 ± 0.02
<i>ube1c</i>	0.99 ± 0.04	0.94 ± 0.02		1.00 ± 0.02	0.99 ± 0.03	1.09 ± 0.04	1.02 ± 0.03		1.09 ± 0.04	0.97 ± 0.03
<i>uchl1</i>	0.95 ± 0.03	0.93 ± 0.02		0.91 ± 0.03	0.97 ± 0.02	1.01 ± 0.04	1.21 ± 0.05		1.09 ± 0.03	1.24 ± 0.05
<i>uchl3</i>	0.96 ± 0.01	0.94 ± 0.01		0.98 ± 0.01	0.95 ± 0.02	1.04 ± 0.02	1.07 ± 0.03		1.05 ± 0.03	1.09 ± 0.02
<i>vav1</i>	1.02 ± 0.19	1.27 ± 0.15		0.97 ± 0.08	1.19 ± 0.16	0.70 ± 0.12	1.03 ± 0.20		0.87 ± 0.06	1.12 ± 0.11
<i>vegf</i>	1.34 ± 0.13	1.38 ± 0.08		1.25 ± 0.15	1.20 ± 0.04	0.57 ± 0.02	0.71 ± 0.06		0.57 ± 0.04	0.71 ± 0.09
<i>vegfb</i>	0.89 ± 0.05	0.93 ± 0.05	*	1.05 ± 0.06	1.00 ± 0.03	0.90 ± 0.04	1.07 ± 0.04	*	0.96 ± 0.05	1.26 ± 0.09
<i>vegfc</i>	0.90 ± 0.05	0.79 ± 0.09		0.99 ± 0.06	0.88 ± 0.04	1.10 ± 0.05	1.09 ± 0.05	*	1.36 ± 0.07	1.25 ± 0.10
<i>vhl</i>	1.00 ± 0.02	1.06 ± 0.02		0.99 ± 0.02	1.07 ± 0.03	1.01 ± 0.02	1.01 ± 0.01	*	0.95 ± 0.01	0.95 ± 0.02
<i>wt1</i>	1.40 ± 0.52	1.89 ± 0.47	†	1.34 ± 0.35	0.56 ± 0.16†	0.98 ± 0.29	1.33 ± 0.30		1.62 ± 0.42	1.30 ± 0.22

Normalized expression ratios are given as mean ± SE obtained from five independent cultures in each group, with the sample from each culture run on a separate array. Several of the values reported in this table have appeared in previous studies of other gene groupings [1,3-7,9,10].

*Significant main treatment effect in two-factor ANOVA (treatment, time).

†Interaction of treatment × time; then, † denotes significant treatment effect for a given time point.

Global statistical analysis of Table 3: ANOVA factors of treatment, differentiation state, gene, time[§]

Treatment × gene, p < 0.0001; treatment × state, p < 0.03; treatment × gene × time, p < 0.0003; treatment × gene × state, p < 0.0001; treatment × gene × state × time, p < 0.0001

Undifferentiated: treatment main effect (Control > CPF), p < 0.005; treatment × gene, p < 0.0001; treatment × gene × time, p < 0.005

Differentiating: treatment × gene, p < 0.0001; treatment × gene × time, p < 0.0001

[§]results shown include only treatment effects and interactions of treatment with other variables

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