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## Supplemental Material

# Binding and Activity of Tetrabromobisphenol A Mono-Ether Structural Analogs to Thyroid Hormone Transport Proteins and Receptors

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**Figure S1.** Cytotoxicity of the tetrabromobisphenol A (TBBPA) mono-ether structural analogs [TBBPA-mono(glycidyl ether) (TBBPA-MGE), TBBPA-mono(allyl ether) (TBBPA-MAE) and TBBPA-mono(2,3-dibromopropyl ether) (TBBPA-MDBPE)], the TBBPA bis-ether derivatives [TBBPA-bis(glycidyl ether) (TBBPA-BGE), TBBPA-bis(allyl ether) (TBBPA-BAE) and TBBPA-bis(2,3-dibromopropyl ether) (TBBPA-BDBPE)] and TBBPA determined by Cell Counting Kit-8 (CCK-8) assay. GH3 cells were treated with different concentrations of the tested chemicals. Three replicated wells were included for each group in a 96-well plate. The error bar represents the standard deviation of three replicates. * $p < 0.05$, compared with cell samples of the control group (0.1% dimethyl sulfoxide). The $p$ values of the experimental data were analyzed using one-way analysis of variance (ANOVA), followed by a least significant difference multiple comparisons test (IBM SPSS Statistics 20). See the summary data in Table S1.

**Figure S2.** Competitive binding curves of the tetrabromobisphenol A (TBBPA) mono-ether structural analogs [TBBPA-mono(glycidyl ether) (TBBPA-MGE), TBBPA-mono(allyl ether) (TBBPA-MAE) and TBBPA-mono(2,3-dibromopropyl ether) (TBBPA-MDBPE)], the TBBPA bis-ether derivatives [TBBPA-bis(glycidyl ether) (TBBPA-BGE), TBBPA-bis(allyl ether) (TBBPA-BAE) and TBBPA-bis(2,3-dibromopropyl ether) (TBBPA-BDBPE)] and TBBPA with thyroxine-binding globulin (TBG). Three replicate wells were conducted for each group in a 96-well plate. Error bars represent the standard deviation of three replicates. *$p < 0.05$, compared with the control group (1% dimethyl sulfoxide). The $p$ values of the experimental data were analyzed using one-way analysis of variance (ANOVA), followed by a least significant difference multiple comparisons test (IBM SPSS Statistics 20). See the summary data in Table S3.

**Figure S3.** The interactions of tetrabromobisphenol A (TBBPA) mono-ether structural analogs [TBBPA-mono(glycidyl ether) (TBBPA-MGE), TBBPA-mono(allyl ether) (TBBPA-MAE) and TBBPA-mono(2,3-dibromopropyl ether) (TBBPA-MDBPE)] and TBBPA with transthyretin (TTR).

**Figure S4.** Competitive binding curves of the tetrabromobisphenol A (TBBPA) mono-ether structural analogs [TBBPA-mono(glycidyl ether) (TBBPA-MGE), TBBPA-mono(allyl ether) (TBBPA-MAE) and TBBPA-mono(2,3-dibromopropyl ether) (TBBPA-MDBPE)], the TBBPA bis-ether derivatives [TBBPA-bis(glycidyl ether) (TBBPA-BGE), TBBPA-bis(allyl ether) (TBBPA-BAE) and TBBPA-bis(2,3-dibromopropyl ether) (TBBPA-BDBPE)] and TBBPA with thyroid hormone receptor β-ligand binding domain (TRβ-LBD). Three replicate wells were conducted for each group in a 96-well plate. Error bars represent the standard deviation of three replicates. * $p < 0.05$, compared with the control group (1% dimethyl sulfoxide). The $p$ values of the experimental data were analyzed using one-way analysis of variance (ANOVA), followed by a least significant difference multiple comparisons test (IBM SPSS Statistics 20). See the summary data in Table S6.

**Figure S5.** Overlay of the binding modes of the tetrabromobisphenol A (TBBPA) mono-ether structural analogs [TBBPA-mono(glycidyl ether) (TBBPA-MGE), TBBPA-mono(allyl ether) (TBBPA-MAE) and TBBPA-mono(2,3-dibromopropyl ether) (TBBPA-MDBPE)] with TBBPA in human thyroid hormone receptor β-ligand binding domain (TRβ-LBD). The protein is shown in green. TBBPA is shown in blue. TBBPA mono-ether structural analogs are shown in gray.

**Figure S6.** The interactions of tetrabromobisphenol A (TBBPA) mono-ether structural analogs [TBBPA-mono(glycidyl ether) (TBBPA-MGE), TBBPA-mono(allyl ether) (TBBPA-MAE) and TBBPA-mono(2,3-dibromopropyl ether) (TBBPA-MDBPE)] and TBBPA with thyroid hormone receptor α-ligand binding domain (TRα-LBD).

**Figure S7.** The interactions of tetrabromobisphenol A (TBBPA) mono-ether structural analogs [TBBPA-mono(glycidyl ether) (TBBPA-MGE), TBBPA-mono(allyl ether) (TBBPA-MAE) and TBBPA-mono(2,3-dibromopropyl ether) (TBBPA-MDBPE)] and TBBPA with thyroid hormone receptor β-ligand binding domain (TRβ-LBD).

**Table S1.** Summary data for Figure S1. “SD” means standard deviation of three replicates.

**Table S2.** Summary data for Figure 2. “RBP” means relative binding potency. “SD” means standard deviation of three replicates.

**Table S3.** Summary data for Figure S2. “RBP” means relative binding potency. “SD” means standard deviation of three replicates.

**Table S4.** The results of docking scores and interactions of tetrabromobisphenol A (TBBPA) mono-ether structural analogs [TBBPA-mono(glycidyl ether) (TBBPA-MGE), TBBPA-mono(allyl ether) (TBBPA-MAE) and TBBPA-mono(2,3-dibromopropyl ether) (TBBPA-MDBPE)] and TBBPA with transthyretin (TTR).

**Table S5.** Summary data for Figure 4. “RBP” means relative binding potency. “SD” means standard deviation of three replicates.

**Table S6.** Summary data for Figure S4. “RBP” means relative binding potency. “SD” means standard deviation of three replicates.

**Table S7.** The results of docking scores and interactions of tetrabromobisphenol A (TBBPA) mono-ether structural analogs [TBBPA-mono(glycidyl ether) (TBBPA-MGE), TBBPA-mono(allyl ether) (TBBPA-MAE) and TBBPA-mono(2,3-dibromopropyl ether) (TBBPA-MDBPE)] and TBBPA with thyroid hormone receptor α-ligand binding domain (TRα-LBD).

**Table S8.** The results of docking scores and interactions of tetrabromobisphenol A (TBBPA) mono-ether structural analogs [TBBPA-mono(glycidyl ether) (TBBPA-MGE), TBBPA-mono(allyl ether) (TBBPA-MAE) and TBBPA-mono(2,3-dibromopropyl ether) (TBBPA-MDBPE)] and TBBPA with thyroid hormone receptor β-ligand binding domain (TRβ-LBD).

**Table S9.** Summary data for Figure 5. “RCP” means relative cell proliferation compared with dimethyl sulfoxide control group. “SD” means standard deviation of three replicates.

**Table S10.** Summary data for Figure 6. “RCP” means relative cell proliferation compared with dimethyl sulfoxide control group. “SD” means standard deviation of three replicates.