Supporting Information

Red clover aryl hydrocarbon receptor (AhR) and estrogen receptor (ER) agonists enhance estrogen genotoxic metabolism

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Figure Legends

Figure S1. LC-MS/MS analysis of methoxyestrone metabolites (2-MeOE$_1$, 4-MeOE$_1$) in MCF-10A cells. A) Cells were treated with RC (10 µg/mL) and compounds, GN, DZ, BA, FN (10 µM) for 48 h and then 24 h with E$_2$ (1 µM).

Figure S2. TCDD-induced XRE-luciferase reporter activity in HC-04 and MCF-7 cells. A) XRE-luciferase reporter activity was analyzed after 24 h treatment with TCDD (10 nM) in HC-04 cells and MCF-7 cells. Results were analyzed by t-test to compare TCDD treatment to DMSO treatment, *p < 0.05.

Figure S3. LC-MS/MS analysis of TCDD-induced methoxy ether metabolites (2-MeOE$_1$, 4-MeOE$_1$) and CYP1A1/1B1 expression in MCF-10A and MCF-7 cells. Levels of 2-MeOE$_1$ and 4-MeOE$_1$ metabolites from A) MCF-10A and B) MCF-7 cells were analyzed by LC-MS/MS after 48 h treatment with TCDD (10 nM) then 24 h with E$_2$ (1 µM). CYP1A1 and CYP1B1 expression levels were determined after 24 h treatment with TCDD (10 nM) in C) MCF-10A and D) MCF-7 cells by RT-qPCR analysis. Results were analyzed by t-test to compare TCDD treatment to DMSO treatment, *p < 0.05.

Figure S4. CYP1A1/1B1 expression levels in MCF-7 cells after treatment with E$_2$. A) Cells were treated with E$_2$ (1 nM, 1 µM) for 24 h before RT-qPCR analysis of CYP1A1 and B) CYP1B1 levels.

Figure S5. CYP1A1 and CYP1B1 expression levels in MCF-7 cells after cotreatment with isoflavones and E$_2$. RT-qPCR analysis of A) CYP1A1 and B) CYP1B1 expression levels after 24 h cotreatment of MCF-7 cells with isoflavones (10 µM) and E$_2$ (1 nM) and C) CYP1A1 and D) CYP1B1 expression levels were determined after 24 h cotreatment of MCF-7 cells with isoflavones (10 µM) and E$_2$ (1 µM).
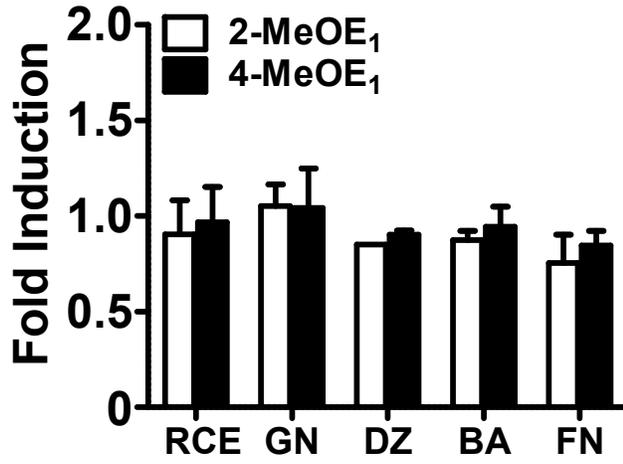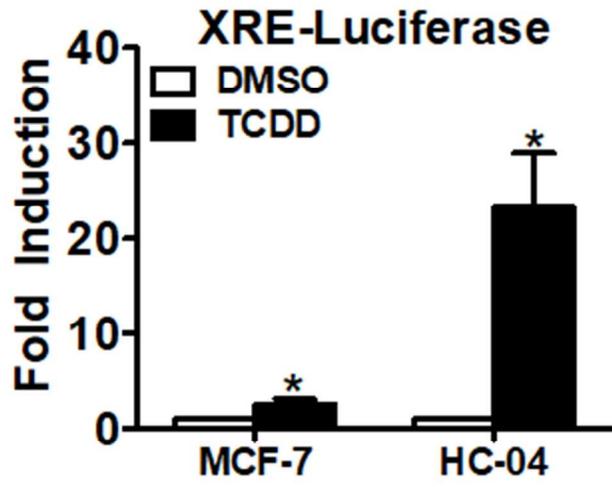
1   **Figure S1**

Fold Induction for 2-MeOE$_1$ and 4-MeOE$_1$ across RCE, GN, DZ, BA, and FN.

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1 **Figure S2**

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1 **Figure S3**
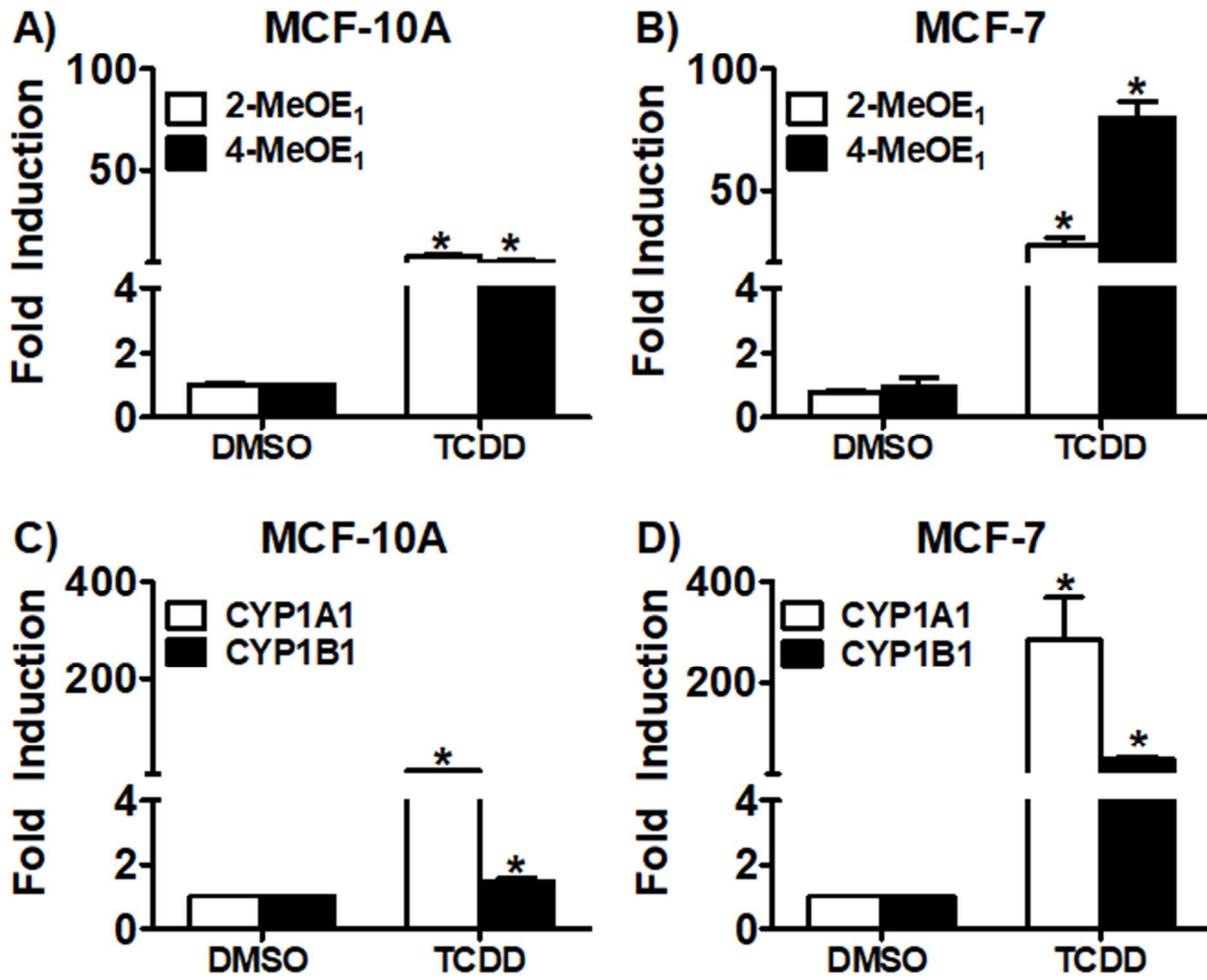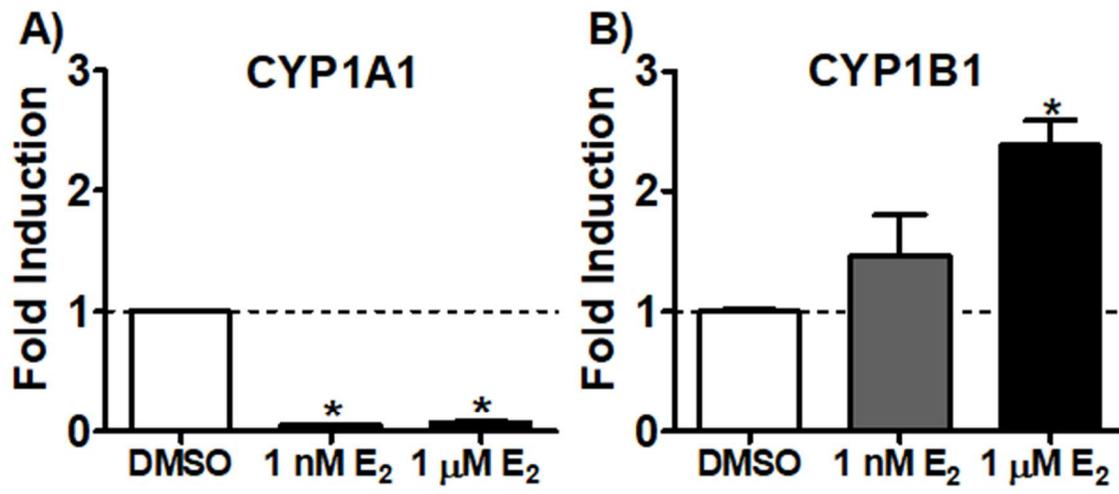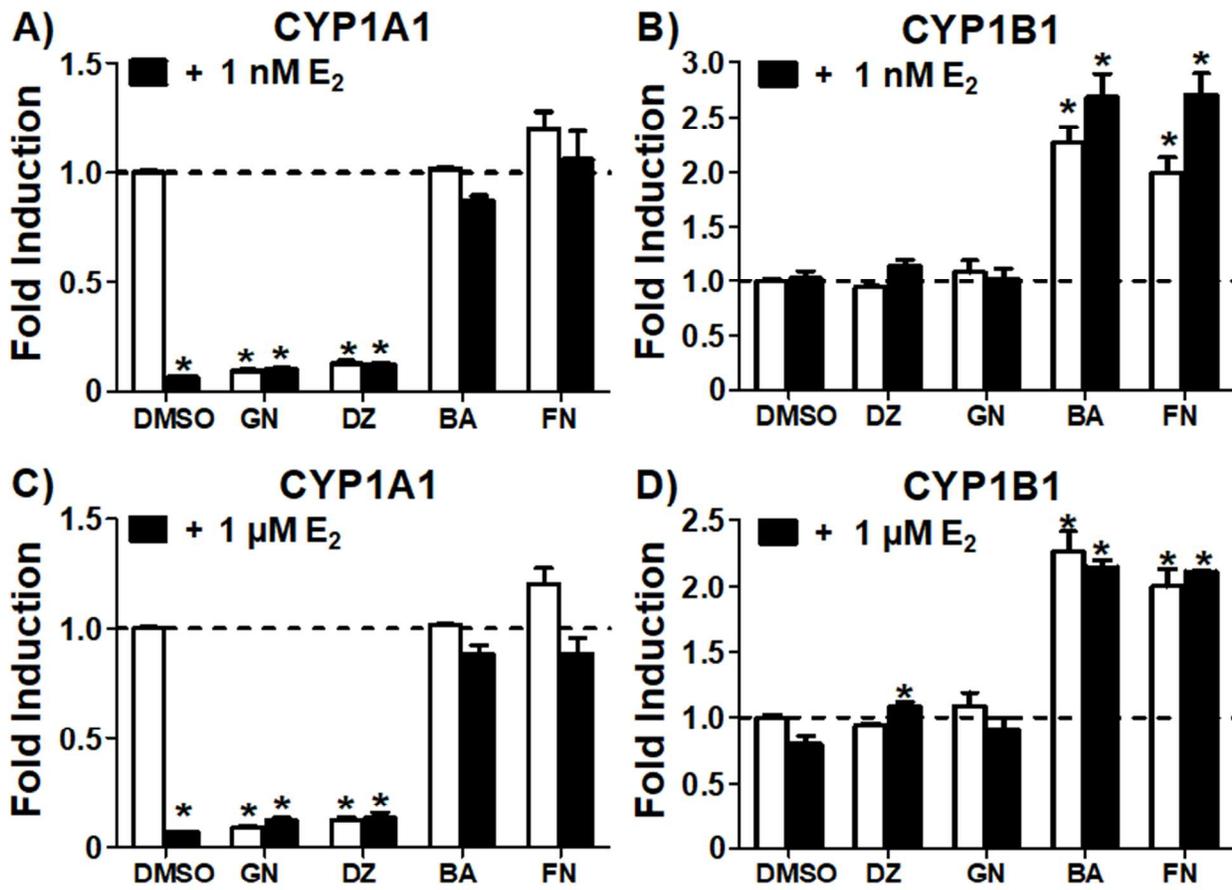

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1   **Figure S4**

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Figure S5