

## Membrane estrogen receptor $\alpha$ signaling modulates the sensitivity to estradiol treatment in a dose- and tissue- dependent manner

Yiwen Jiang<sup>1#</sup>, Karin Horkeby<sup>1#\*</sup>, Petra Henning<sup>1</sup>, Jianyao Wu<sup>1</sup>, Lina Lawenius<sup>1</sup>, Cecilia Engdahl<sup>1,3</sup>, Priti Gupta<sup>1,3</sup>, Sofia Movérare-Skrtic<sup>1</sup>, Karin H Nilsson<sup>1</sup>, Ellis Levin<sup>4</sup>, Claes Ohlsson<sup>1,2</sup>, Marie K Lagerquist<sup>1</sup>

**Supplementary Table 1.** Stable serum E2 levels in high-dose E2 treated groups throughout the experiment.

Timepoint	WT-E2	C451A-E2	Šídák's multiple comparisons test
1-week	184±13 (n=6)	193±29 (n=5)	ns
2-week	226±20 (n=5)	330±32 (n=3)	ns
3-week	260±33 (n=10)	209±34 (n=8)	ns

(Two-way ANOVA analysis: interaction: ns; timepoint: ns; genotype: ns)

Ovariectomized WT and C451A females were treated with 17beta-estradiol (E2) of 6  $\mu\text{g}/\text{mouse}/\text{day}$  for three weeks. Serum samples were taken after 1-week, 2-week and 3-week of treatment, and serum E2 levels were measured by LC-MS. Two-way ANOVA followed by Šídák's multiple comparisons test was applied for analysis. All values are presented as mean  $\pm$  SEM. ns; not significant.