



**Supplementary Figure S1. E2 in standard fetal bovine serum (FBS) and stripped serum.** E2 was measured by liquid chromatography with triple quad mass spectrometer (LC-MS/MS; LCMS-8050, Shimadzu). For E2 measurement,  $17\beta$ -Estradiol-2, 4, 16, 16-d<sub>4</sub> are added to serum sample as internal standards. Samples are pretreated using Isolute SLE+ prior to analysis and derivatized with 0.1 M Sodium bicarbonate and 1 mg/mL (acetone) Dansyl Chloride 1 mg/mL. Phase separation on a Acquity UPLC BEH C18 (1.7  $\mu$ m  $\times$  2.1  $\times$  50 mm) column (Waters) was performed using 0.1% formic acid in water and methanol, 60  $^{\circ}$ C. The analytical measuring range (AMR) for E2 is over 0.07 nM. FBS is obtained from biowest and treated with/without "Stripping serum" method. Data presented as mean  $\pm$  SD (n=3) are representative of at least three independent experiments. \*\*\*\* $P$  < 0.0001 versus control (no E2) using unpaired t test.