

**Supplemental Fig.1** GJIC assay in MDA-MB-435 cells with LY294002 10  $\mu$ M in the presence or absence of 5% fetal bovine serum. Although the magnitude of LY294002 was slightly increased in the presence of serum the overall effect was not altered.

**Supplemental Fig.2** Structure of LY294002 and LY303511.

**Supplemental Fig.3** GJIC assay using the casein kinase 2 (CK2) inhibitors

4,5,6,7-Tetrabromo-2-azabenzimidazole (TBB) (Sigma #T0826) 1.0  $\mu$ M and Tyrphostin AG 1112 (Tyr 1112) (Sigma #T6193) 10  $\mu$ M. No increases were observed with CK2 inhibition compared to LY294002 or LY303511 indicating that the increase in GJIC from LY294002/LY303511 treatments is not due to inhibition of CK2.

**Supplemental Fig.4** GJIC assay with  $Ca^{2+}$  inhibition in MDA-MB-435. (A) Xestospongine C

(Xes.C) (Sigma#X2628) 0.5  $\mu$ M, 0.1  $\mu$ M, 2.0  $\mu$ M was used to inhibit the IP3 receptor and block  $Ca^{2+}$  flux from the endoplasmic reticulum in the presence of LY294002. Co-treatment of cells with LY294002 and Xes.C did not cause a decrease in the effect of LY294002. (B)

1,2-Bis(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid tetrakis-acetoxymethyl ester (BAPTA) (Sigma #A1076) 5  $\mu$ M, 10  $\mu$ M was used to chelate intracellular  $Ca^{2+}$  stores in the presence of LY294002. No decrease in the effect of LY294002 was observed in the presence of BAPTA, supporting the fact that LY294002 does not change GJIC by altering intracellular  $Ca^{2+}$  levels.