# Supporting Information

**Gorrini et al. 10.1073/pnas.1324136111**

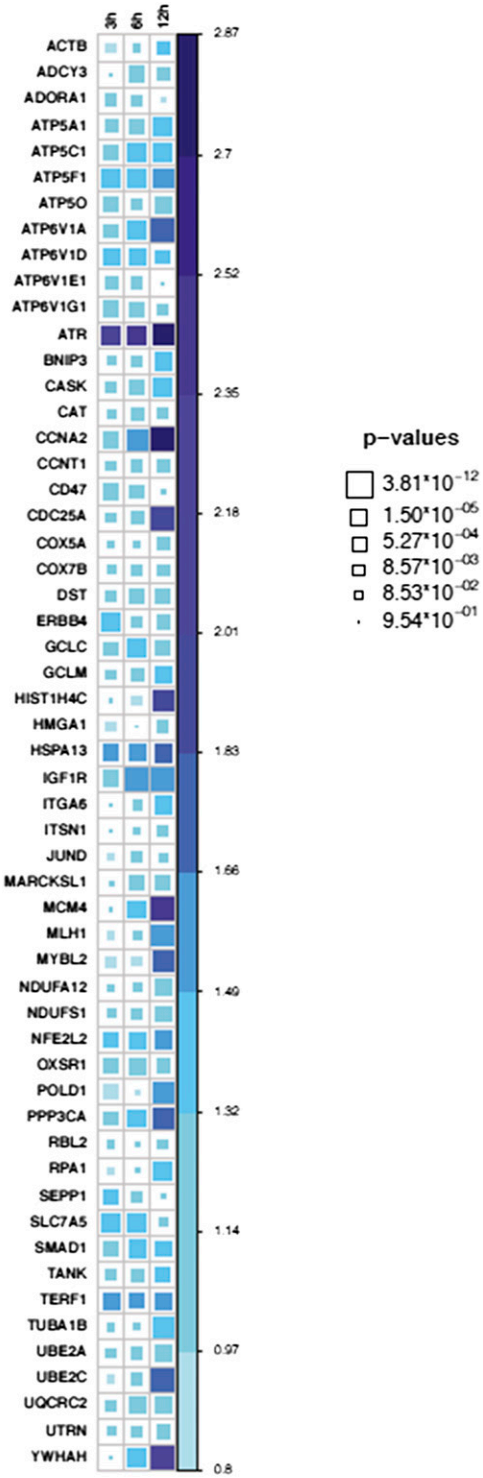

**Fig. S1.** E2 regulates various reactive oxygen species (ROS)-related pathways. MCF7 cells were treated with 100 nM E2 for 0, 3, 6, or 12 h. At each time point, mRNA levels of the indicated ROS-related genes were measured by microarray analysis. Data are the fold change calculated relative to the mRNA level in the control group (0 h; set to 1). Statistical significance was determined at a false discovery rate of 5%. Data are available from the NCBI GEO database (accession no. GSE11324).

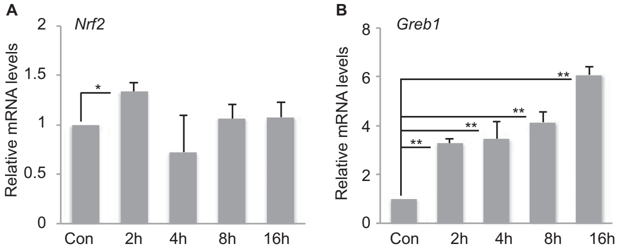

**Fig. S2.** E2 does not affect NRF2 mRNA expression. (*A* and *B*) HC11 were E2-treated for different times as indicated. NRF2 (*A*) and GREB1 (*B*) mRNA levels were analyzed. Error bars illustrate standard error. $*P < 0.05$ and $**P < 0.01$.

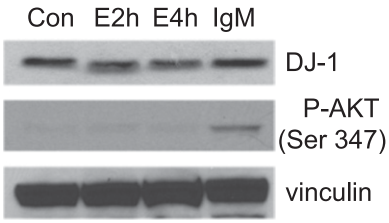

**Fig. S3.** E2 does not activate PI3K signaling in B cells. Freshly isolated B cells were E2 treated or stimulated with IgM Ig. AKT phosphorylation and DJ-1 accumulation were analyzed by Western blotting. Vinculin, loading control.

**Table S1. Detailed analysis of GOTERM_BP_FAT annotation cluster of E2-regulated genes shown in Fig. S1**

| Term | Count | Percent | *P* value | Benjamini |
|---|---|---|---|---|
| GO:0006796~phosphate metabolic process | 18 | 32.72727273 | 6.36E-08 | 1.00E-05 |
| GO:0006793~phosphorus metabolic process | 18 | 32.72727273 | 6.36E-08 | 1.00E-05 |
| GO:0016310~phosphorylation | 16 | 29.09090909 | 1.90E-07 | 2.25E-05 |
| GO:0007049~cell cycle | 13 | 23.63636364 | 2.87E-05 | 0.001045501 |
| GO:0006091~generation of precursor metabolites and energy | 11 | 20 | 2.55E-07 | 2.68E-05 |
| GO:0006259~DNA metabolic process | 10 | 18.18181818 | 1.17E-04 | 0.003814571 |
| GO:0022402~cell cycle process | 10 | 18.18181818 | 2.68E-04 | 0.007433458 |
| GO:0042592~homeostatic process | 10 | 18.18181818 | 0.00204282 | 0.04849184 |
| GO:0006119~oxidative phosphorylation | 9 | 16.36363636 | 3.29E-09 | 1.56E-06 |
| GO:0006163~purine nucleotide metabolic process | 9 | 16.36363636 | 4.93E-07 | 3.60E-05 |
| GO:0006812~cation transport | 9 | 16.36363636 | 0.001139564 | 0.029579348 |
| GO:0022403~cell cycle phase | 9 | 16.36363636 | 1.66E-04 | 0.005067176 |
| GO:0015992~proton transport | 8 | 14.54545455 | 3.04E-09 | 2.88E-06 |
| GO:0006818~hydrogen transport | 8 | 14.54545455 | 3.83E-09 | 1.21E-06 |
| GO:0046034~ATP metabolic process | 8 | 14.54545455 | 1.39E-07 | 1.89E-05 |
| GO:0009205~purine ribonucleoside triphosphate metabolic process | 8 | 14.54545455 | 2.93E-07 | 2.78E-05 |
| GO:0009199~ribonucleoside triphosphate metabolic process | 8 | 14.54545455 | 3.11E-07 | 2.68E-05 |
| GO:0009144~purine nucleoside triphosphate metabolic process | 8 | 14.54545455 | 3.90E-07 | 3.08E-05 |
| GO:0009141~nucleoside triphosphate metabolic process | 8 | 14.54545455 | 6.33E-07 | 4.29E-05 |
| GO:0009150~purine ribonucleotide metabolic process | 8 | 14.54545455 | 9.00E-07 | 5.69E-05 |
| GO:0009259~ribonucleotide metabolic process | 8 | 14.54545455 | 1.38E-06 | 7.68E-05 |
| GO:0006164~purine nucleotide biosynthetic process | 8 | 14.54545455 | 1.44E-06 | 7.59E-05 |
| GO:0009165~nucleotide biosynthetic process | 8 | 14.54545455 | 6.58E-06 | 2.71E-04 |
| GO:0034654~nucleobase, nucleoside, nucleotide and nucleic acid biosynthetic process | 8 | 14.54545455 | 8.39E-06 | 3.18E-04 |
| GO:0034404~nucleobase, nucleoside and nucleotide biosynthetic process | 8 | 14.54545455 | 8.39E-06 | 3.18E-04 |
| GO:0015672~monovalent inorganic cation transport | 8 | 14.54545455 | 2.00E-04 | 0.005916916 |
| GO:0044271~nitrogen compound biosynthetic process | 8 | 14.54545455 | 2.29E-04 | 0.006554106 |
| GO:0015985~energy coupled proton transport, down electrochemical gradient | 7 | 12.72727273 | 8.32E-09 | 1.97E-06 |
| GO:0015986~ATP synthesis coupled proton transport | 7 | 12.72727273 | 8.32E-09 | 1.97E-06 |
| GO:0034220~ion transmembrane transport | 7 | 12.72727273 | 2.95E-08 | 5.60E-06 |
| GO:0006754~ATP biosynthetic process | 7 | 12.72727273 | 1.09E-06 | 6.47E-05 |
| GO:0009206~purine ribonucleoside triphosphate biosynthetic process | 7 | 12.72727273 | 1.93E-06 | 9.61E-05 |
| GO:0009201~ribonucleoside triphosphate biosynthetic process | 7 | 12.72727273 | 2.04E-06 | 9.69E-05 |
| GO:0009145~purine nucleoside triphosphate biosynthetic process | 7 | 12.72727273 | 2.04E-06 | 9.69E-05 |
| GO:0009142~nucleoside triphosphate biosynthetic process | 7 | 12.72727273 | 2.44E-06 | 1.10E-04 |
| GO:0009152~purine ribonucleotide biosynthetic process | 7 | 12.72727273 | 5.41E-06 | 2.33E-04 |
| GO:0009260~ribonucleotide biosynthetic process | 7 | 12.72727273 | 7.57E-06 | 2.99E-04 |
| GO:0006260~DNA replication | 7 | 12.72727273 | 8.44E-05 | 0.002853686 |
| GO:0000279~M phase | 7 | 12.72727273 | 0.001568772 | 0.038410327 |
| GO:0000279~M phase | 7 | 12.72727273 | 0.001568772 | 0.038410327 |
| GO:0042391~regulation of membrane potential | 6 | 10.90909091 | 1.58E-04 | 0.004989659 |
| GO:0006261~DNA-dependent DNA replication | 4 | 7.272727273 | 0.001423991 | 0.03585247 |
| GO:0051899~membrane depolarization | 4 | 7.272727273 | 5.93E-04 | 0.015941235 |