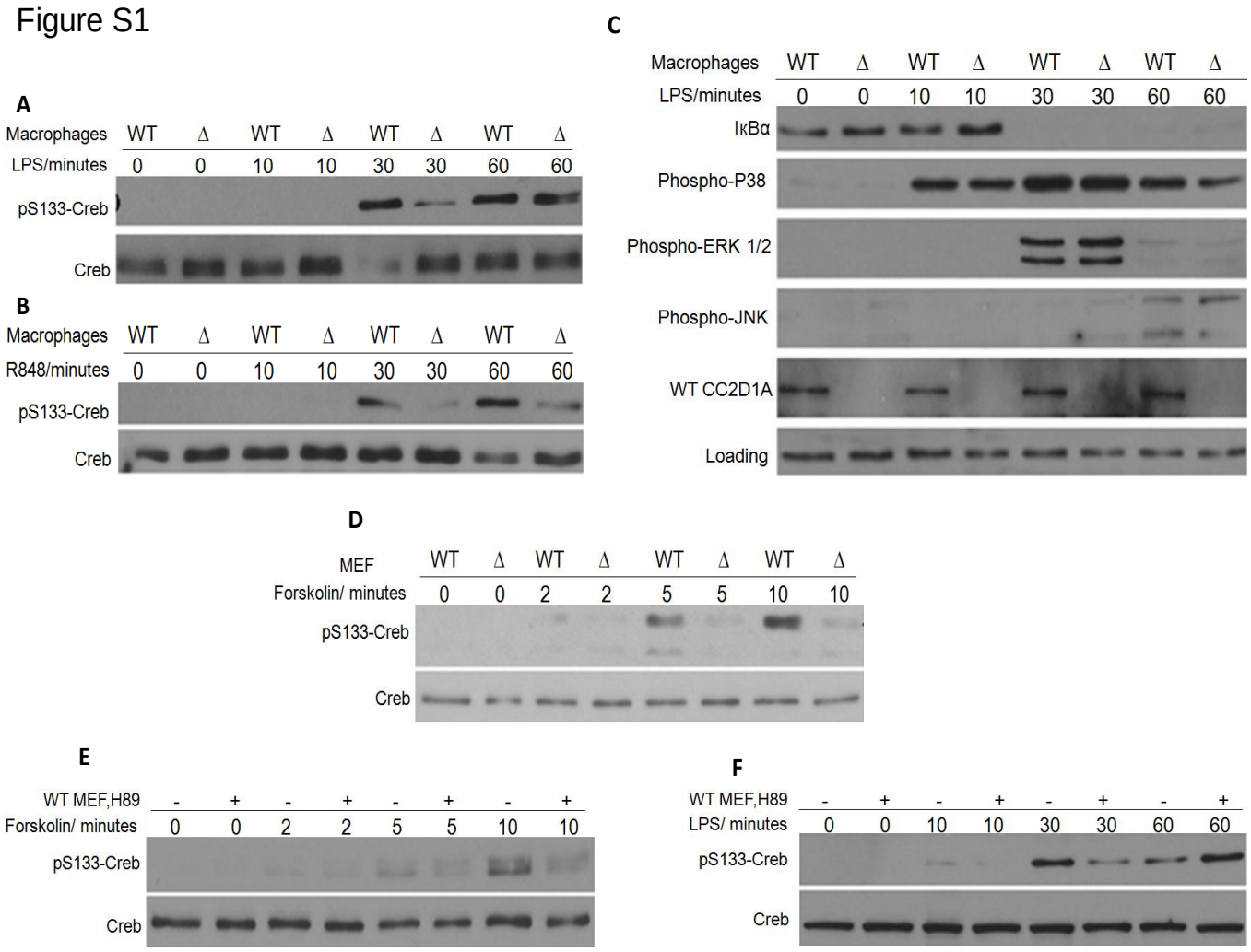
SUPPLEMENTAL FIGURES

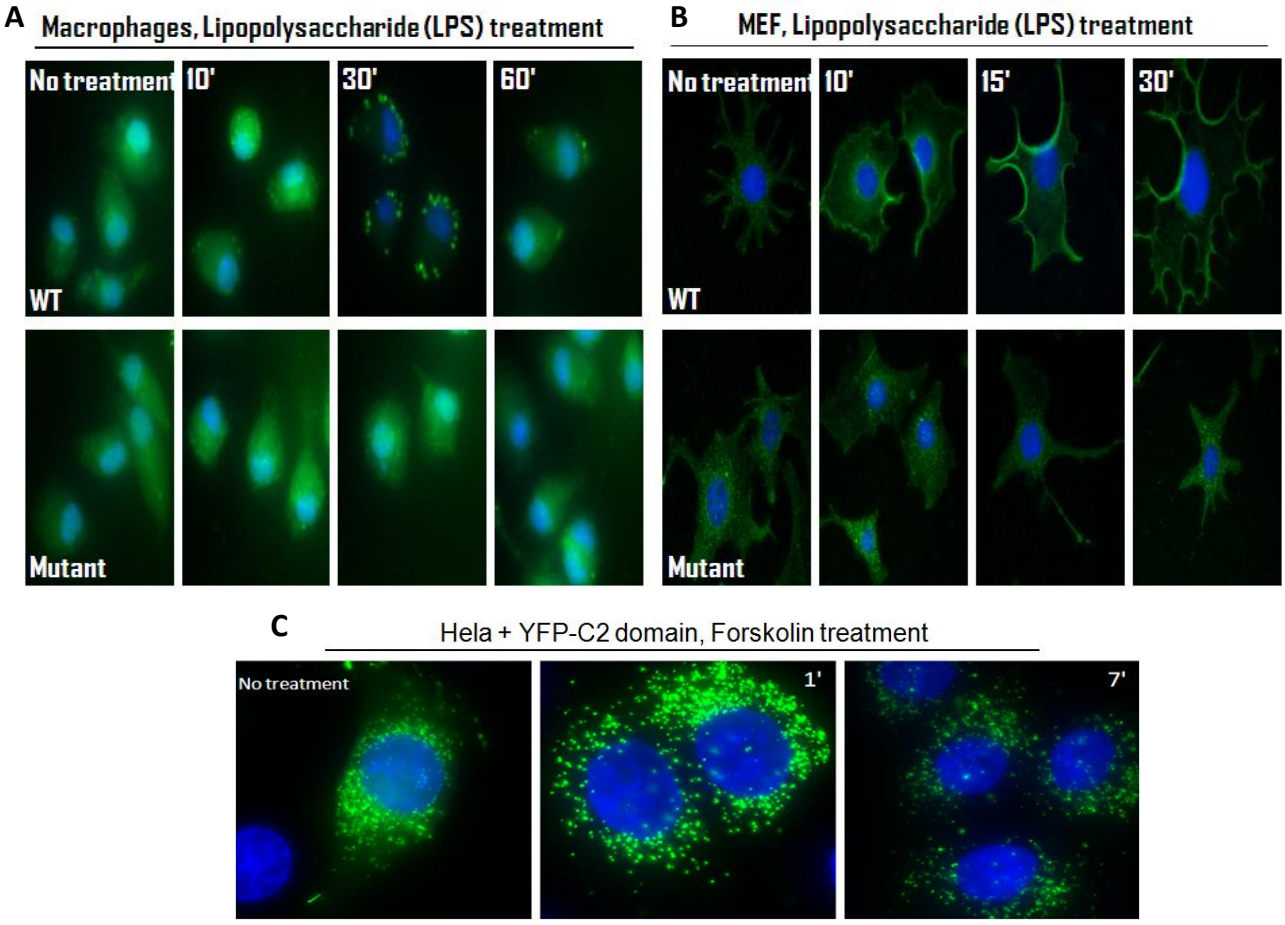


<u>Figure S1</u>. CREB phosphorylation at S133 is defective in *CC2D1A* mutant cells.

A and ***B***, Western blots of S133 phosphorylation of CREB in response to LPS (1ug/ml) or R848 (1ug/ml)treatment in WT and mutant macrophage cells. ***C***, WB of IκBα, MAP kinase phosphorylation (p38, ERK, JNK) in response to LPS treatment in WT and mutant macrophage cells. ***D***, WB of S133 phosphorylation of CREB in response to forskolin (50uM) treatment in WT and *CC2D1A* mutant MEF cells (used in Figure 4A). ***E*** and ***F***, WB of S133 phosphorylation of CREB in response to forskolin or LPS treatment. WT MEF cells were cultured and treated

with PKA inhibitor H89 (30uM) and then with forskolin or LPS. In all cases cells were collected, washed with PBS and lysed in 1x RIPA buffer with protease inhibitors. Twenty ug protein was loaded from each lysate for WB analyses.

Figure S2



<u>Figure S2</u>. Subcellular localization of the Cc2d1a protein in response to increases in cAMP. ***A***, Immunostaining shows Cc2d1a protein localization to cortical puncta in WT macrophages after stimulation with LPS. ***B***, Immunostaining shows accumulation of Cc2d1a protein toward the cell periphery in WT MEF cells after stimulation with LPS. In both cases the localization phenotype does is not apparent in the *CC2D1A* mutant cells neither before nor after stimulation. ***C***, Images of Hela cells show localization of the transfected YFP-Cc2d1a C2 fusion protein to

cortical puncta before and after stimulation with forskolin. In A and B cells were fixed and analyzed by immuno-fluorescence using an anti-Cc2d1a antibody and DAPI to stain nucleus. Deacon microscopy was used for imaging.