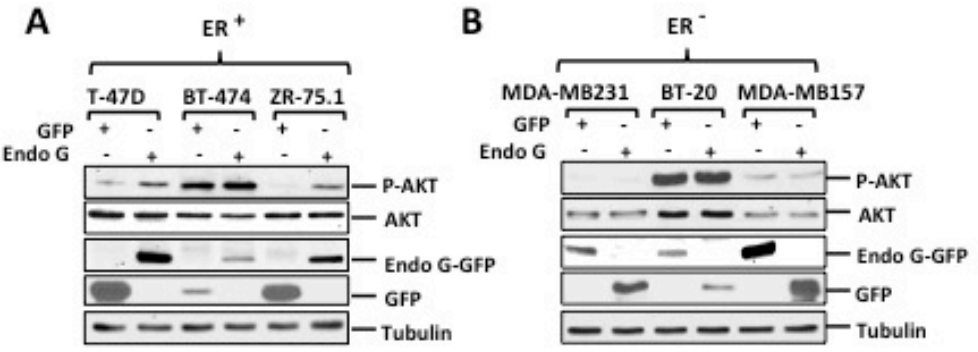

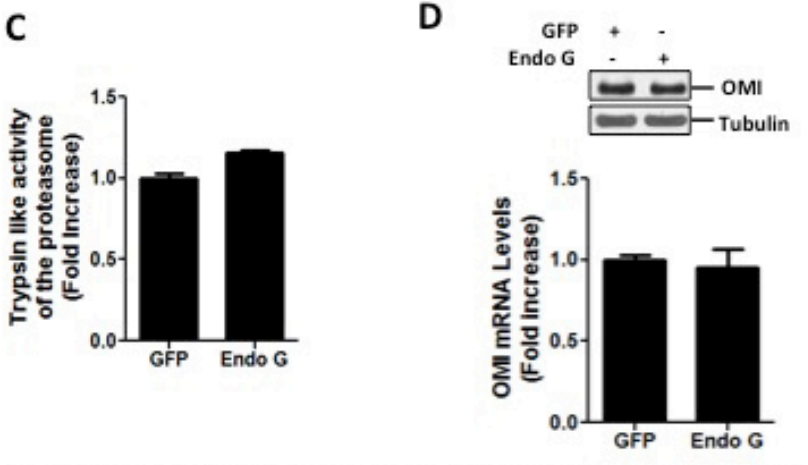

Figure S1. ERα-negative breast cancer cells fail to activate AKT and the outcomes of the ERα- arm of the UPR^{mt} in response to proteotoxic stress. **(A)** Phosphorylation of AKT (Ser473) was evaluated in a panel of ERα-positive cell lines transiently transfected with the indicated plasmids. Levels of the endogenous AKT as well as the exogenous Endo G and GFP were tested by western blotting using anti-AKT and GFP antibody, respectively. **(B)** Cellular crude extracts from a panel of ERα-negative cell lines transfected as indicated were examined as described in A. **(C)** Proteosomal trypsin-like activities were assayed in cells overexpressing either the control GFP or mutant EndoG–GFP as described in the Materials and Methods section. **(D)** Transcript levels of OMI were evaluated by qRT PCR in MDA-MB 231 cells transfected with the indicated plasmids for 24hrs. Data represent the mean ⁺SD of mRNA in transfected cells relative to control cells. Omi levels were detected by western blotting.

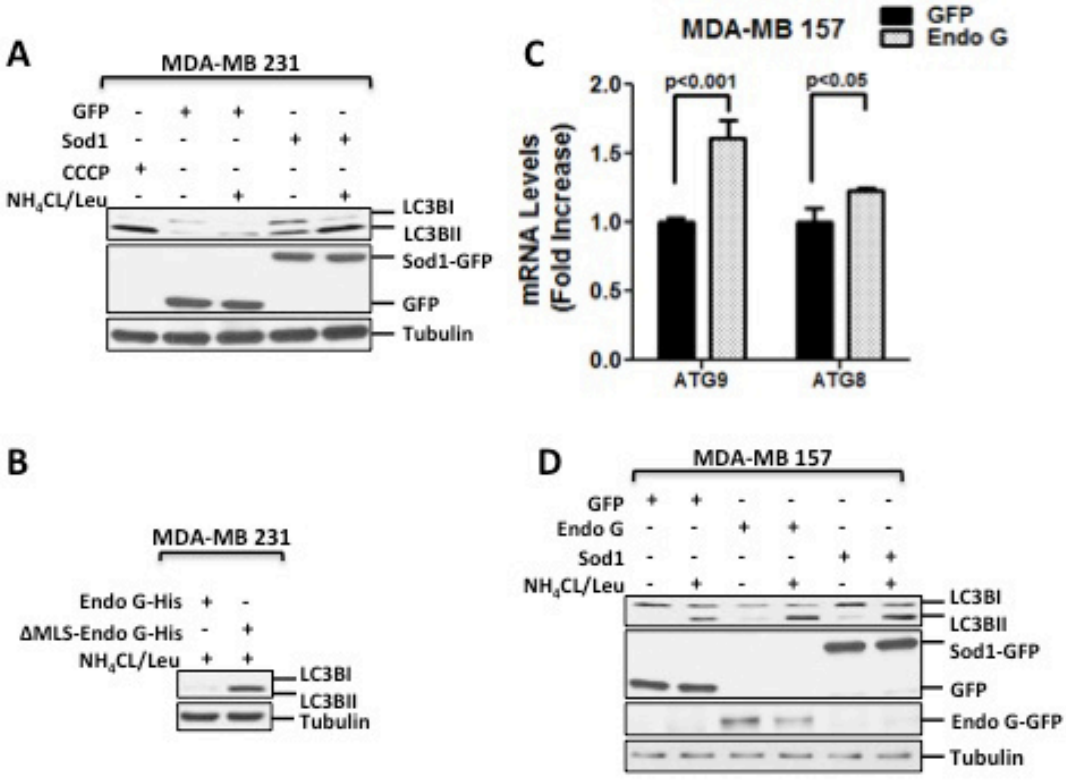

Figure S2. Autophagy is triggered by a variety of misfolded mitochondrial proteins. **(A)** MDA-MB 231 cells were treated with 10μM CCCP overnight or transfected with either mutant SOD1-GFP (G93A) or GFP empty vector for 48hrs followed by treatment with a combination of NH_4CL (20μM) and Leupeptin (0.1 mM) for 3hrs prior to harvesting. Protein extracts were subjected to western blotting to determine levels of lipidated LC3B II. Transfection of GFP and SOD1-GFP was confirmed by western blotting using anti-GFP antibody. **(B)** Crude extracts from MDA-MB 231 cells overexpressing the indicated plasmids in the presence or absence of NH_4CL/Leu combination for 3hrs were analyzed by western blotting at 48hrs time point for levels of lipidated form of LC3B. **(C)** mRNA levels of ATG9 and ATG8 were assessed by qRT PCR in MDA-MB 157 cells transfected as described in A. Data represent the mean ⁺SD of mRNA fold increase relative to control cells. P<0.001; P<0.05 indicates significant increase in mRNA levels in cells transfected with mutant Endo G-GFP versus GFP overexpressing cells. **(D)** Lysates from MDA-MB 157 cells transfected with the indicated plasmids were analyzed by western blotting for lipidated LC3B levels. Transfection of MDA-MB157 cells with GFP, Endo G-GFP and SOD1-GFP was confirmed as described in A.