



**Supplementary Figure 4** Agonist-dependent dissociation of  $\beta_1$ AR/PDE4D complexes does not require  $\beta$ -arrestin. Exogenous  $\beta_1$ AR and PDE4D8-Myc were co-immunoprecipitated from extracts of mouse embryonic fibroblasts derived from mice deficient in  $\beta$ -arrestin 1 and 2 ( $\beta$ arr1/2KO-MEFs) that had been pre-treated for 5 min with or without 100  $\mu$ M Norepinephrine (NE). A representative experiment is reported.