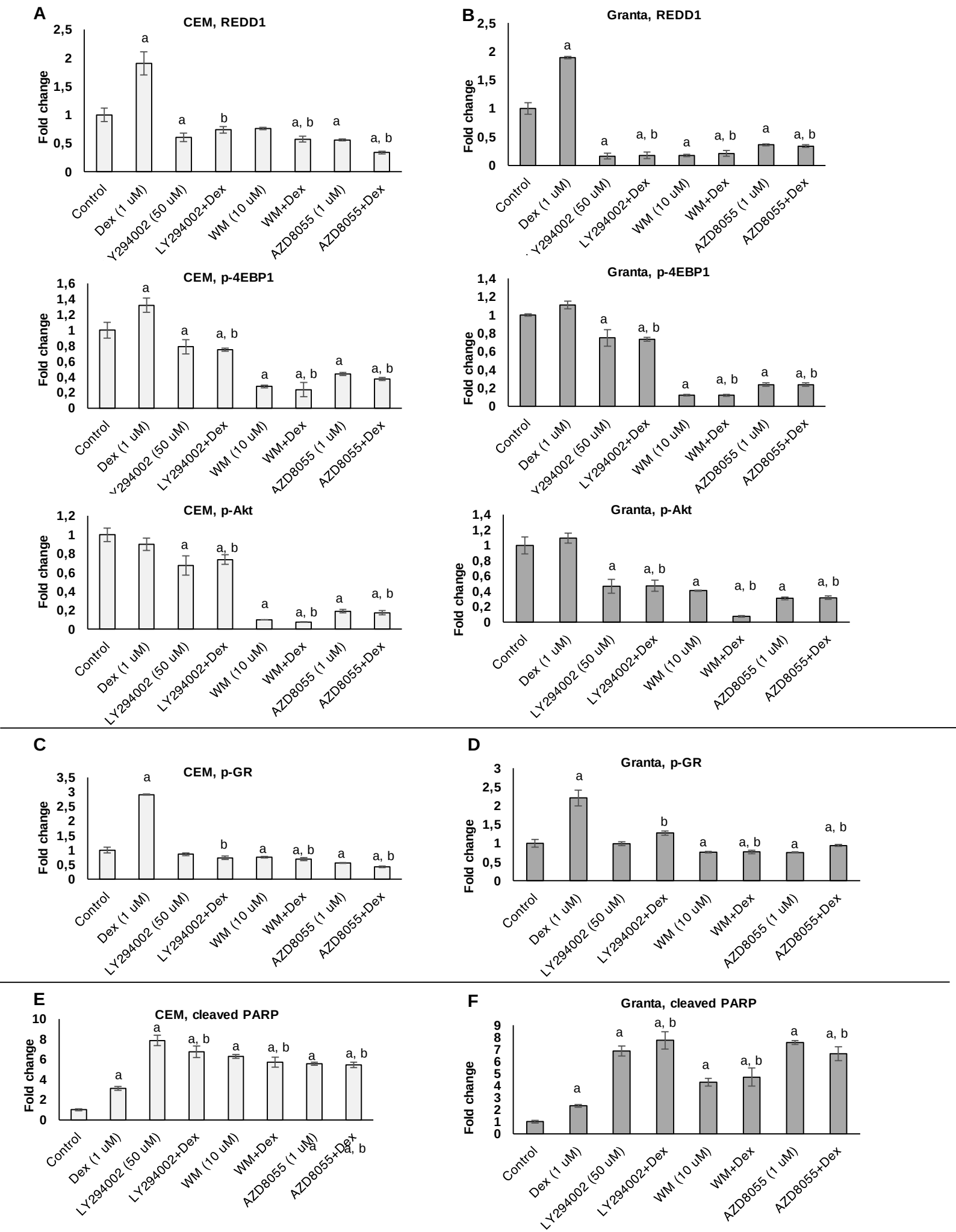
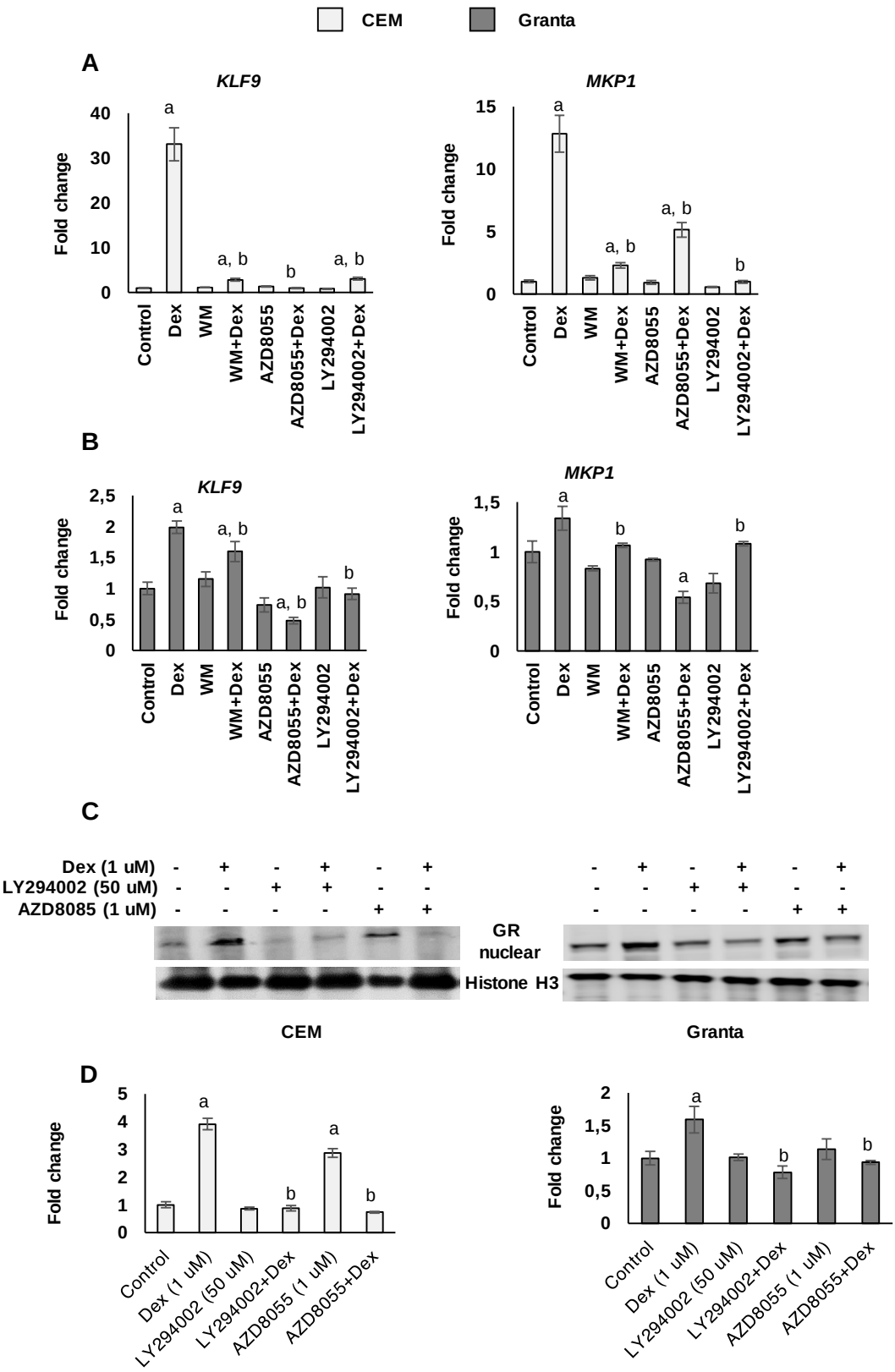
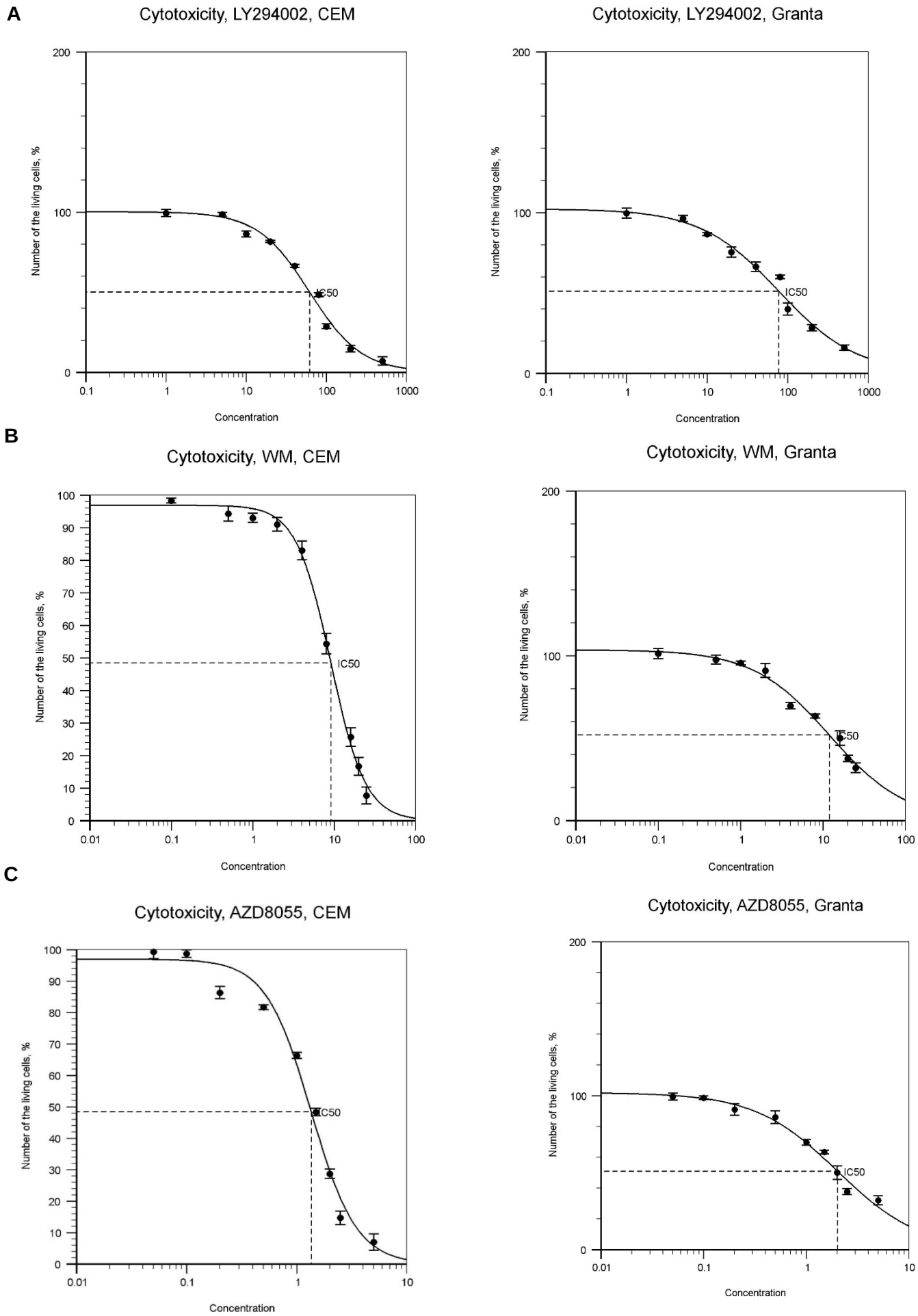


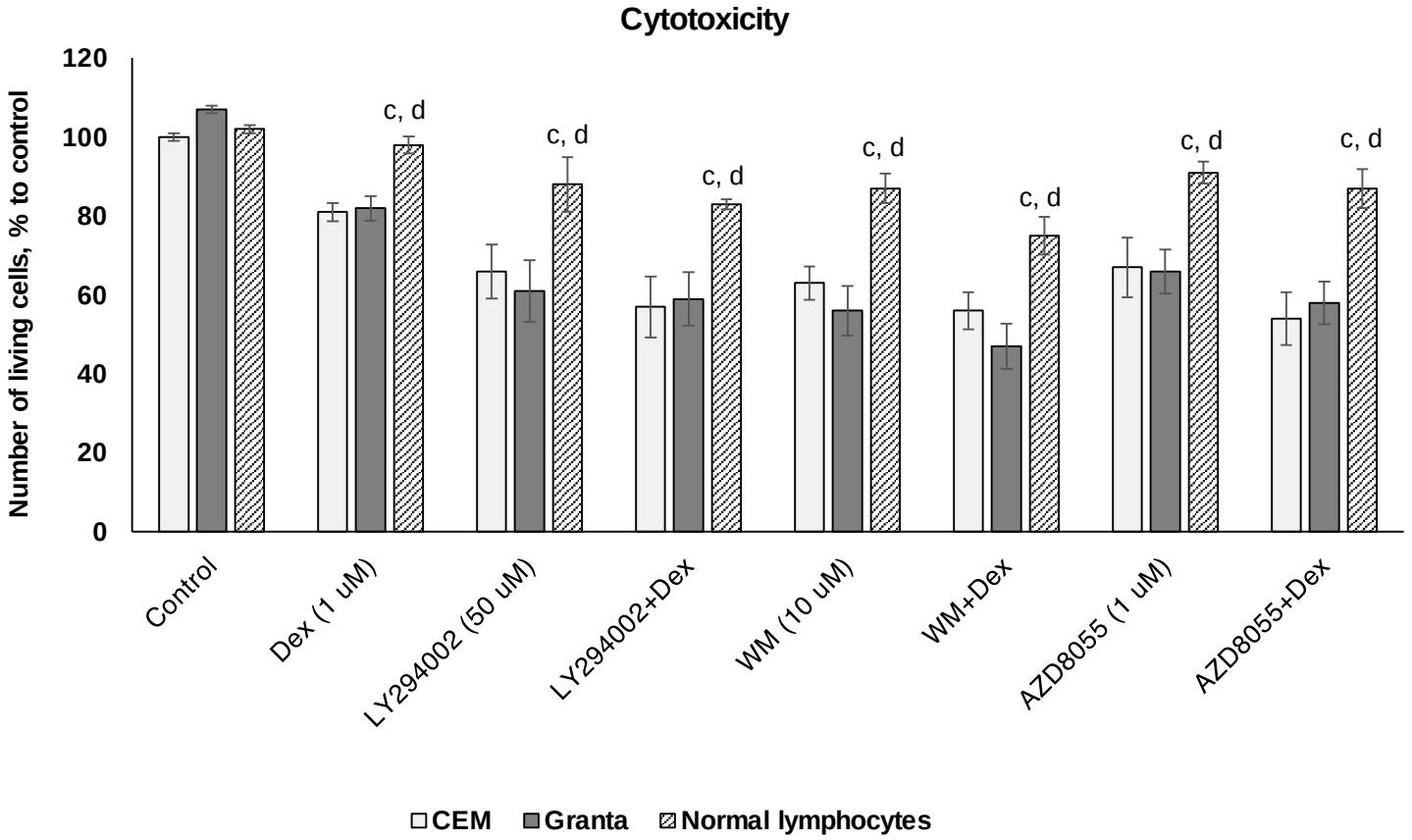
Supplementary Figure 1. Quantification of Western blot analysis. CEM cells (**A, C, E**) and Granta cells (**B, D, F**) were pretreated with solvent (Control), **LY294002** (50 uM), AZD8055 (1 uM) and WM (10 uM) for 6 h and treated with either solvent or glucocorticoid Dex (1 uM) for 24 h. Quantification of Western blot analysis of REDD1, p-4EBP1, p-Akt (**A, B**), p-GR (**C, D**) and cleaved PARP (**E, F**) protein levels was done using Image J free software. Statistically significant differences as compared to: a-control; b-Dex ($p<0.001$) as and where reflected.



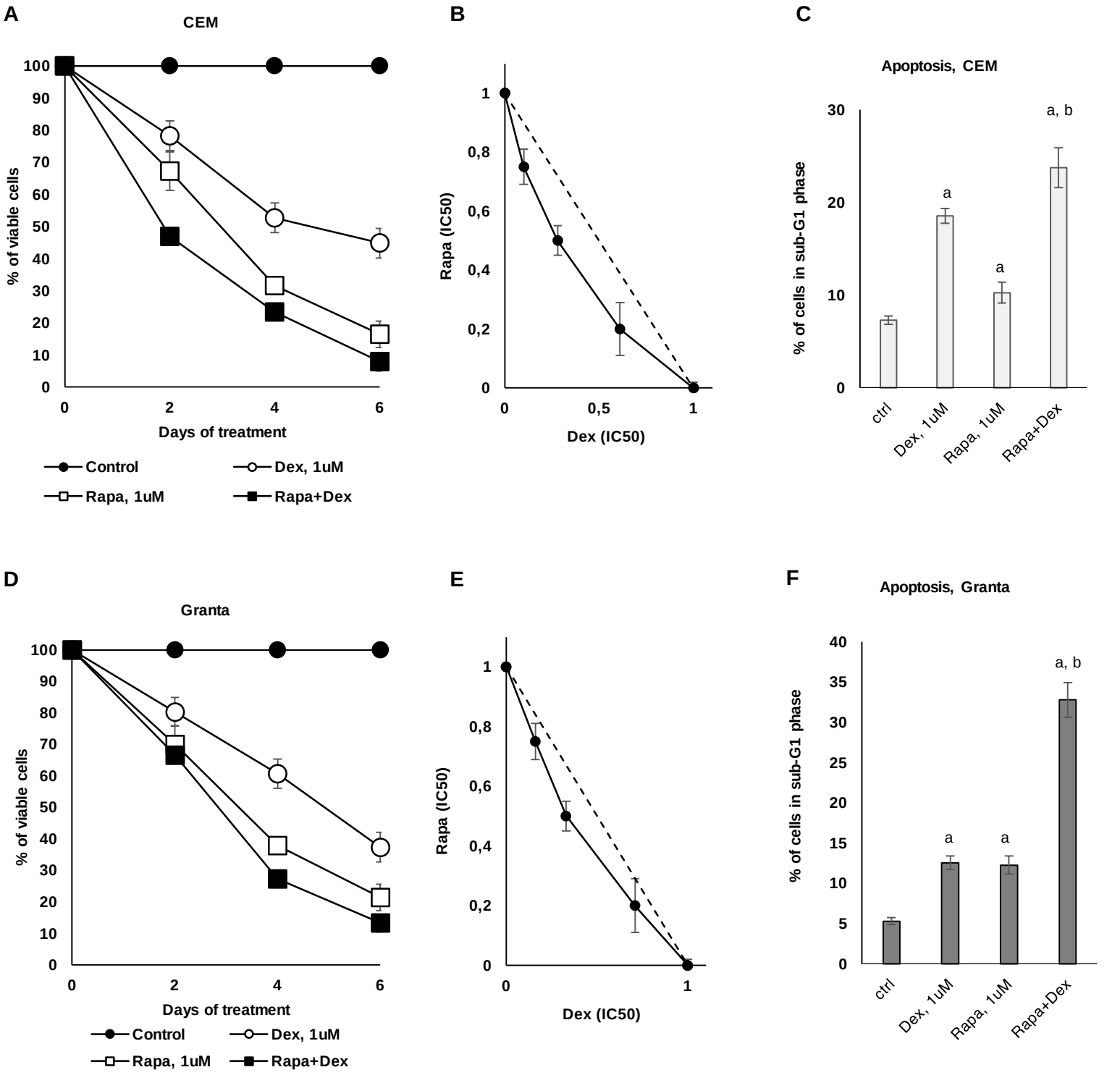
Supplementary Figure 2. Effect of PI3K/mTOR/Akt inhibitors on regulation of endogenous genes by Dex in CEM and Granta cells. CEM (**A**) and Granta (**B**) cells were pretreated with solvent (Control), LY294002 (50 uM), AZD8055 (1 uM) and WM (10 uM) for 6 h and treated with either solvent or glucocorticoid Dex (1 uM) for 24 h. Q-PCR results for TA-associated genes (*KLF9, MKP1*) were normalized to the expression of housekeeping gene *RPL27*. (**C, D**) Western blotting (**C**) of GR nuclear translocation and its densitomeric analysis (**D**). CEM and Granta cells were pretreated with solvent (Control), LY294002 (50 uM) or AZD8055 (1 uM) for 6 h and treated with either solvent or glucocorticoid Dex (1 uM) for 24 h. Histone H3 was used as loading control. Experiments were done in triplicates. Statistically significant differences as compared to: a-control; b-Dex ($p<0.001$) as and where reflected.



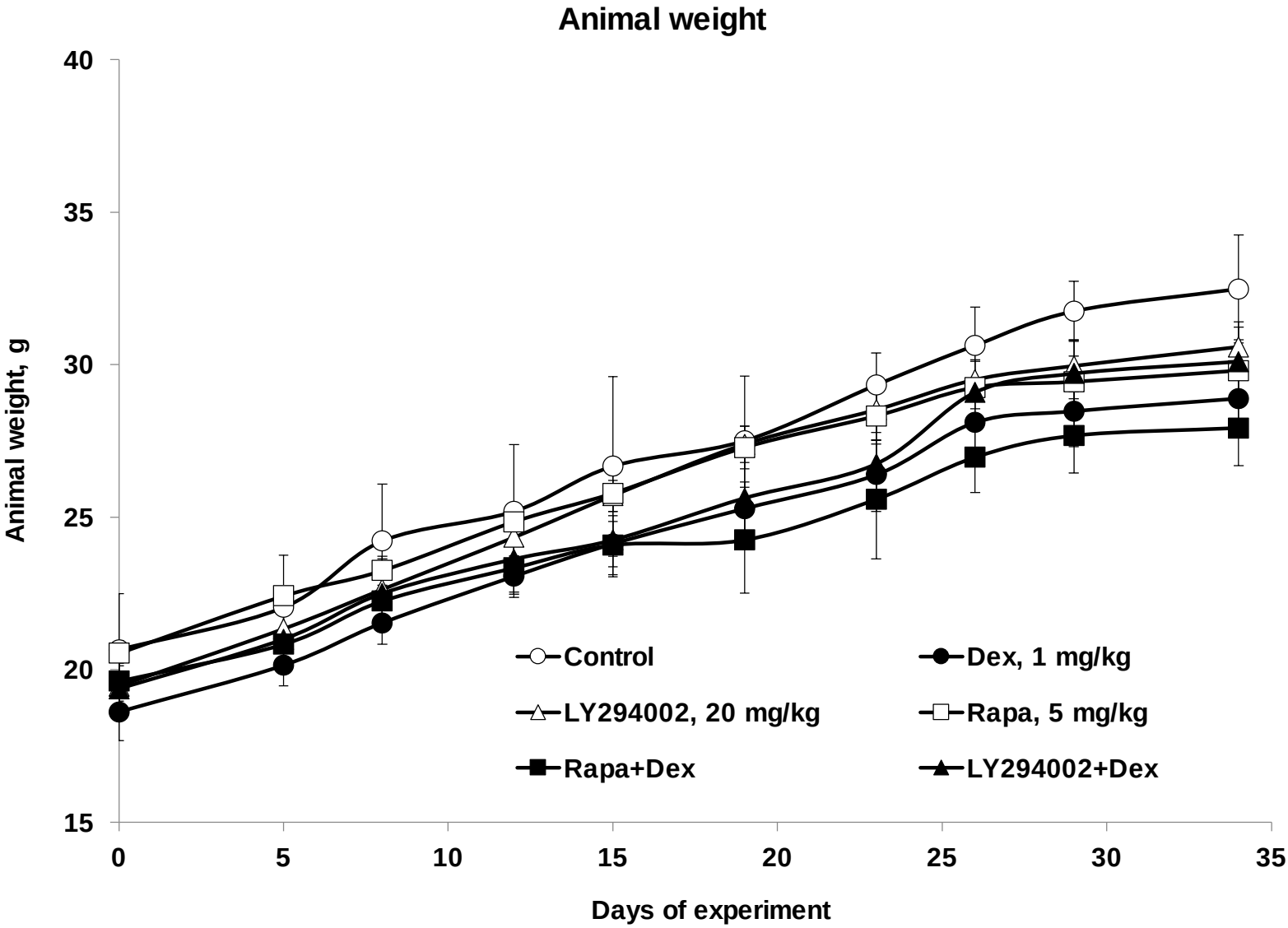
Supplementary Figure 3. Cytotoxic effects of LY294002 (A), Wortmannin (B) and AZD8055 (C) on CEM and Granta cells. CEM and Granta cells were pretreated with solvent (Control), LY294002 (1-500 uM), WM (0,1-25 uM) and AZD8055 (0,05-5 uM) for 6 h and treated with either solvent or glucocorticoid Dex (1 uM) for 24 h. MTT assay was performed in triplets. IC50 values were calculated using Quest Graph IC50 Calculator free software.



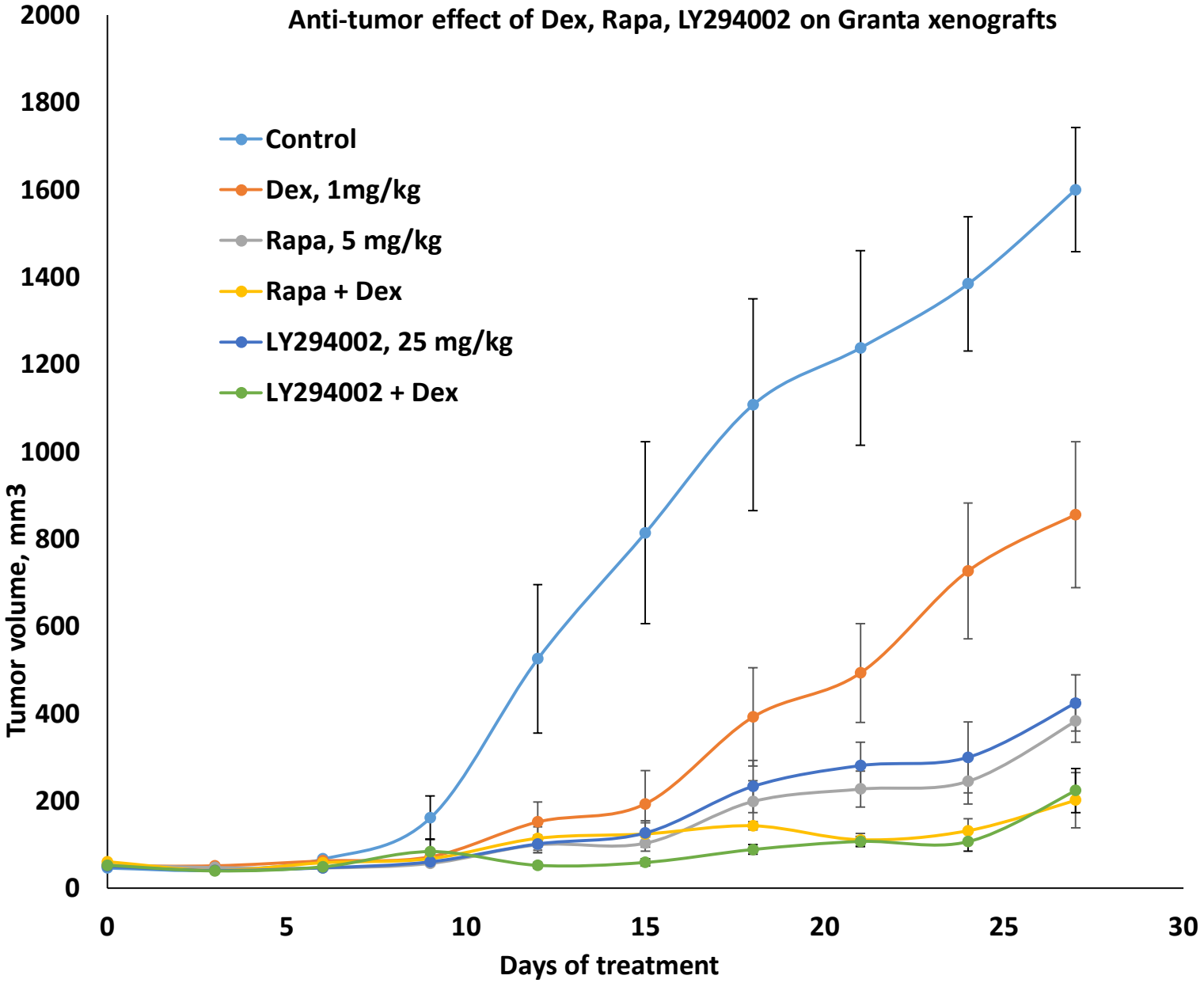
Supplementary Figure 4. Comparative cytotoxic effects of LY294002 (A), Wortmannin (B) and AZD8055 (C) on CEM cells, Granta cells and normal human monocytes. CEM cells, Granta cells and normal human monocytes were pretreated with solvent (Control), LY294002 (50 uM), WM (10 uM) and AZD8055 (1 uM) for 6 h and treated with either solvent or glucocorticoid Dex (1 uM) for 24 h. MTT assay was performed in triplets. Statistically significant differences as compared to: c-CEM cells; d-Granta cells ($p<0.001$) as and where reflected.



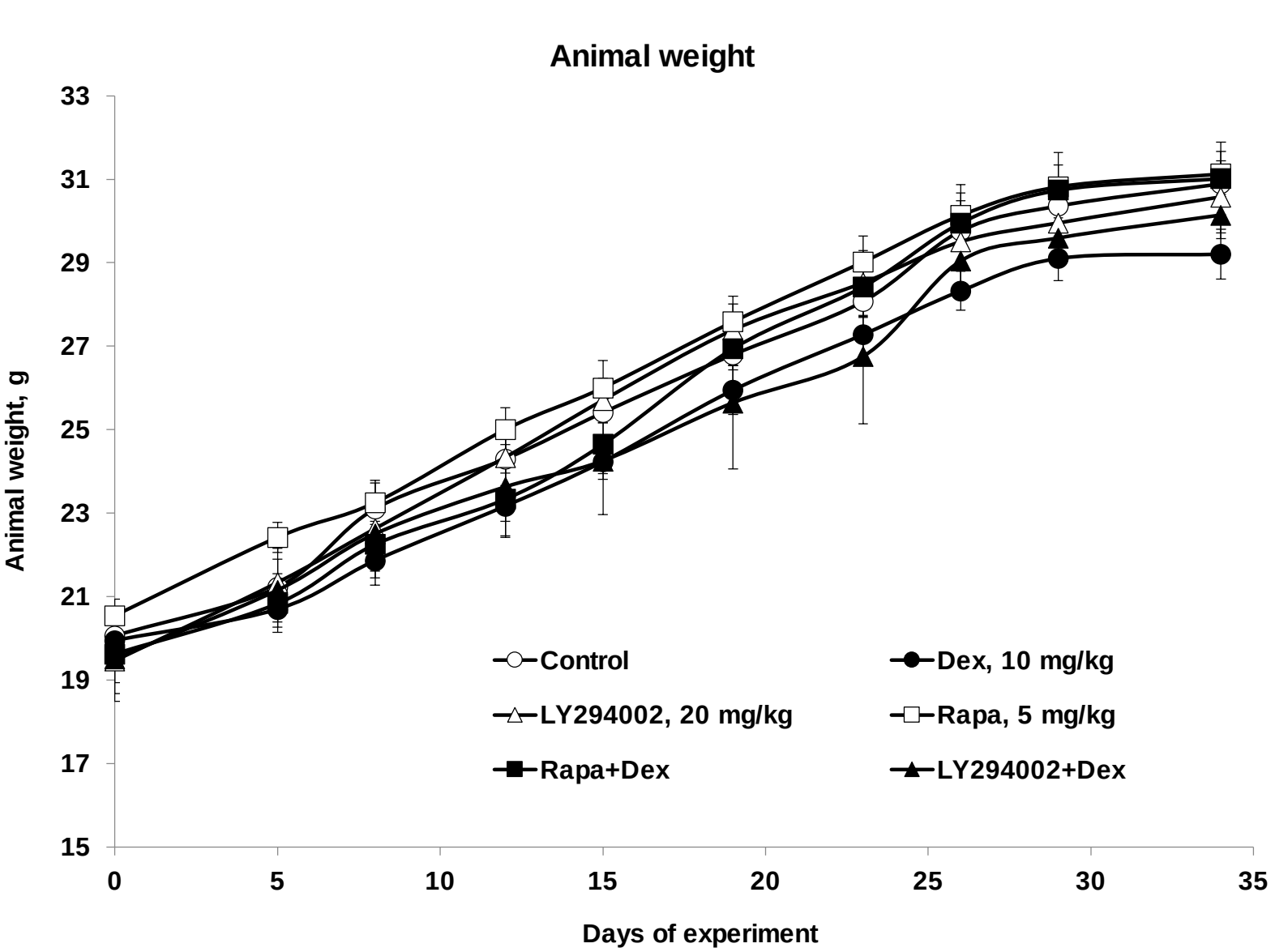
Supplementary Figure 5. Synergistic anti-lymphoma effect of Rapamycin and Dex in CEM and Granta cells. (**A, D**) Cytotoxic effect was determined using MTT assay. CEM (**A**) and Granta (**D**) cells were pretreated with solvent (Control), Rapa (1 uM) for 6 h and treated with either solvent or glucocorticoid Dex (1 uM) for 24-144 h. (**B, E**) Isobologram analysis in CEM (**B**) and Granta (**E**) cells for the combination of Rapa and Dex. The concentration, which produced 50% cell growth inhibition (IC50), is expressed as 1.0 in the ordinate and the abscissa of the isobologram. *Y-axis*, LY294002, AZD8055 or WM (IC50); *X-axis*, Dex (IC50). (**C, F**) Apoptosis induction was evaluated by flow cytometry using PI staining. Statistically significant differences as compared to: a-control; b-Dex ($p<0.001$) as and where reflected.



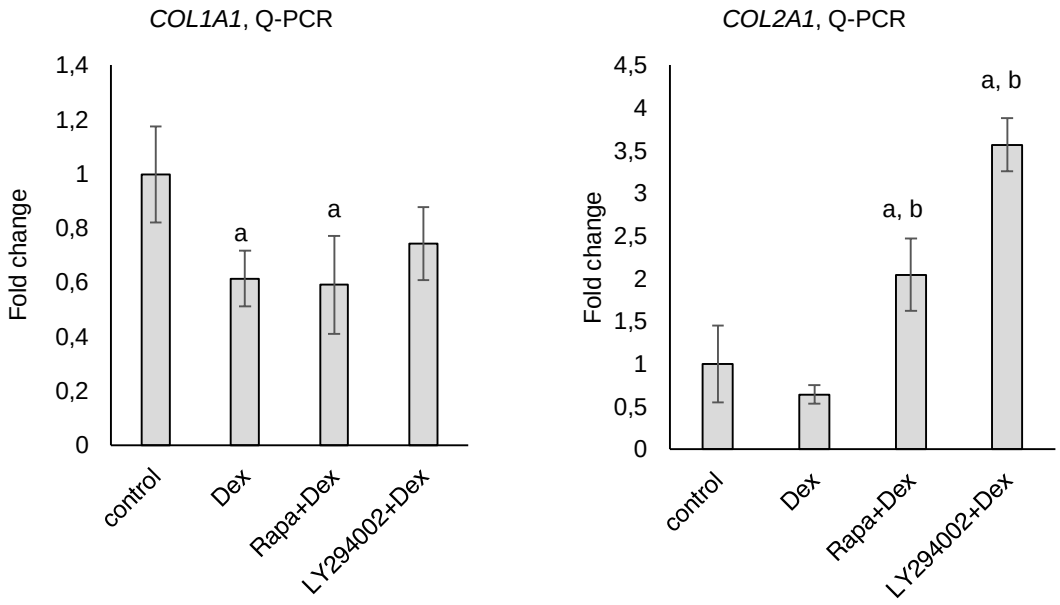
Supplementary Figure 6. Effect of LY294002, Rapamycin and Dex on animal body weight in xenograft study. Granta cells were subcutaneously injected into the right flank of 7 weeks old female nu/nu mice. Animals were randomized and treated i.p. every 48 h with LY294002 (20 mg/kg), Rapamycin (5 mg/kg) of vehicle (30% PEG3350, 4% DMSO, 5% Tween 20 in PBS) followed by Dex (1 mg/kg) of vehicle (5% DMSO in PBS) 6 h later. Body weight was recorded twice a week. Body weight was measured twice a week. There were no statistically significant differences in body weight changes between experimental and control groups.



Supplementary Figure 7. Anti-tumor effect of Dex, Rapa, LY294002 on Granta xenografts. Granta cells were subcutaneously injected into the right flank of 7 weeks old female nu/nu mice. Animals were randomized and treated i.p. every 48 h with LY294002 (20 mg/kg), Rapamycin (5 mg/kg) of vehicle (30% PEG3350, 4% DMSO, 5% Tween 20 in PBS) followed by Dex (1 mg/kg) of vehicle (5% DMSO in PBS) 6 h later. Tumor size was measured twice a week by digital calipers. Treatment groups receiving Rapa or LY294002 individually exhibited statistically significant tumor growth inhibition, relative to the control group, from day 12; treatment groups receiving Rapa or LY294002 in combination with Dex exhibited statistically significant tumor growth inhibition, relative to the control group ($p<0.05$), from day 12, relative to Dex-treated group, from day 21 ($p<0.05$).



Supplementary Figure 8. Effect of LY294002, Rapamycin and Dex on animal body weight in Dexamethasone-induced osteoporosis study. GIOP was induced by i.p. injection of Dex (10 mg/kg) in 12 weeks old BALB/c female mice every 48 h for 5 weeks. 6 h prior to Dex, animals were treated i.p. with LY294002 (20 mg/kg), Rapamycin (5 mg/kg) of vehicle (30% PEG3350, 4% DMSO, 5% Tween-20 in PBS). Body weight was measured twice a week



Supplementary Figure 9. Q-PCR analysis of *Col1a1* and *Col2a1* mRNA expression in bone tissue. GIOP was induced by i.p. injection of Dex (10 mg/kg) in 12 weeks old BALB/c female mice every 48 h for 5 weeks. 6 h prior to Dex, animals were treated i.p. with LY294002 (20 mg/kg), Rapamycin (5 mg/kg) of vehicle (30% PEG3350, 4% DMSO, 5% Tween-20 in PBS). Animals were euthanized 24h after the last Dex treatment. Total RNA from bone tissue was isolated with RiboPure RNA purification kit and cleaned with TURBO DNase. *Col1a1* and *Col2a1* primers were designed with NCBI Primer-BLAST (Supplementary Table 2). Results were normalized to the expression of the housekeeping *RPL27* gene. Statistically significant differences as compared to: a-control; b-Dex ($p<0.001$) as and where reflected**.**