



Figure S7: Roflumilast potentiated the anti-tumor effect of IFN- α *in vivo*. T24 cells (5×10^6 cells/mouse) were subcutaneously injected into BALB/c nude mice. When the tumor size was ~ 150 mm³, mice were treated with phosphate buffered saline (control), roflumilast (75 μ g/kg/day or 5 mg/kg/day, oral administration), and IFN- α (1×10^4 U/mouse/2 days, intraperitoneal injection) either individually or in combination for 28 days before sacrifice. The tumor volumes were measured every 4 days. **(A)** Images of the representative tumors. **(B)** The tumor growth curves of all the treatment groups. Each data point indicates the mean of tumor volume ($n = 7$ per group). **(C)** The tumor weights in all the treatment groups ($n = 7$ per group). **(D)** cAMP levels in tumor tissues of indicated treatment groups. **(E)** The activity of immunoprecipitated PDE4D obtained from tumor tissues of indicated treatment groups. **(F)** PGE₂ concentrations in mice serums of indicated treatment groups. Error bars indicate mean \pm SD ($n = 6$). *, $P < 0.05$; **, $P < 0.01$; #, $P < 0.05$ (*t*-test and Mann-Whitney test).