

**Supplemental Figure 1.** Treatment with PD0325901 leads to a reduction of phospho-Erk. (A) In the colons of mock-treated animals, activation of K-Ras is associated with an increase in phospho-Erk compared to control animals (C). In animals treated for 5, 7, or 13 days with PD0325901 (MEKi), there is a reduction in phospho-Erk. α-Tubulin was used as a loading control. Both control (Fabpl-Cre ; Rosa26-M2-rt-TA ; ColA1-H2B-Egfp) and K-Ras mutant (Fabpl-Cre ; K-Ras<sup>LSL-G12D</sup> ; Rosa26-M2-rtTA ; ColA1-H2B-Egfp) animals (4-6 week old mice at the beginning of treatment) were given a pulse of doxycycline (2mg/ml in water) in the drinking water for 2 weeks. Doxycycline was then removed and animals were treated daily with either PD0325901 (MEKi) or vehicle (DMSO) for either 5, 7, or 13 days following DOX pulse. Animals were then sacrificed and tissue lysate was collected.