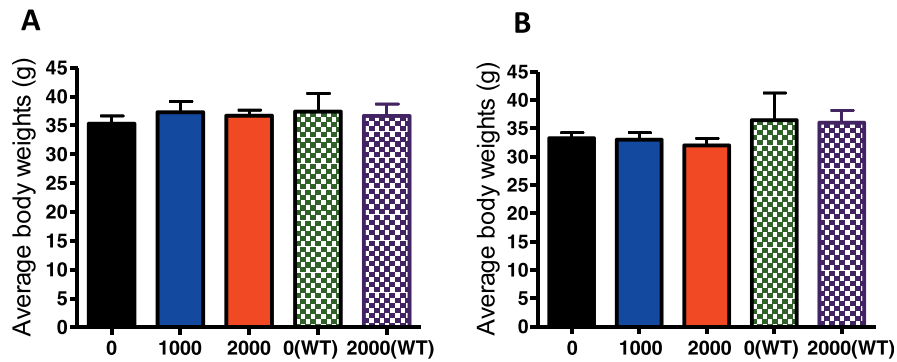
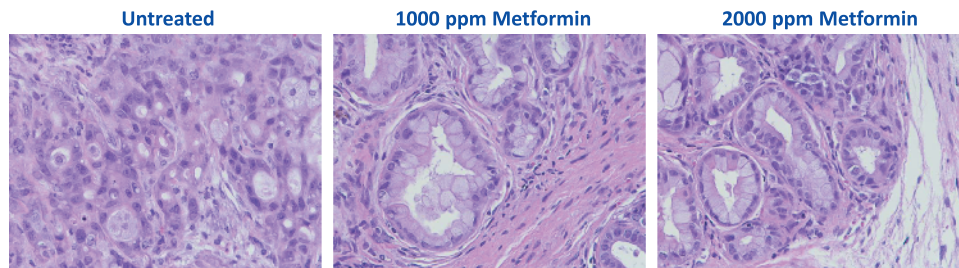


**Figure W1.** Experimental design for evaluation of metformin efficacy in PC prevention in male and female p48<sup>Cre/+</sup>-LSL-Kras<sup>G12D/+</sup> mice. At 6 weeks of age, groups (20-35 per group activated p48<sup>Cre/+</sup>-LSL-Kras<sup>G12D/+</sup> or 12 per group wild-type) of mice were fed AIN-76A diets containing 0-, 1000-, or 2000-ppm metformin continuously for 38 weeks, and each pancreas was evaluated histopathologically for marker expressions as described in the text.



**Figure W2.** (A and B) Effect of metformin on body weights (means  $\pm$  SE) at the termination of the experiment. No statistically significant difference was observed between control and metformin-treated p48<sup>Cre/+</sup>-LSL-Kras<sup>G12D/+</sup> or wild-type mice.



**Figure W3.** Histopathologic analysis of untreated and metformin-treated pancreata using H&E staining. Untreated pancreata show poorly differentiated adenocarcinoma with some of the cells invading the stroma (left panel). Pancreata treated with 1000- and 2000-ppm metformin show PanIN lesions (middle and right panels).