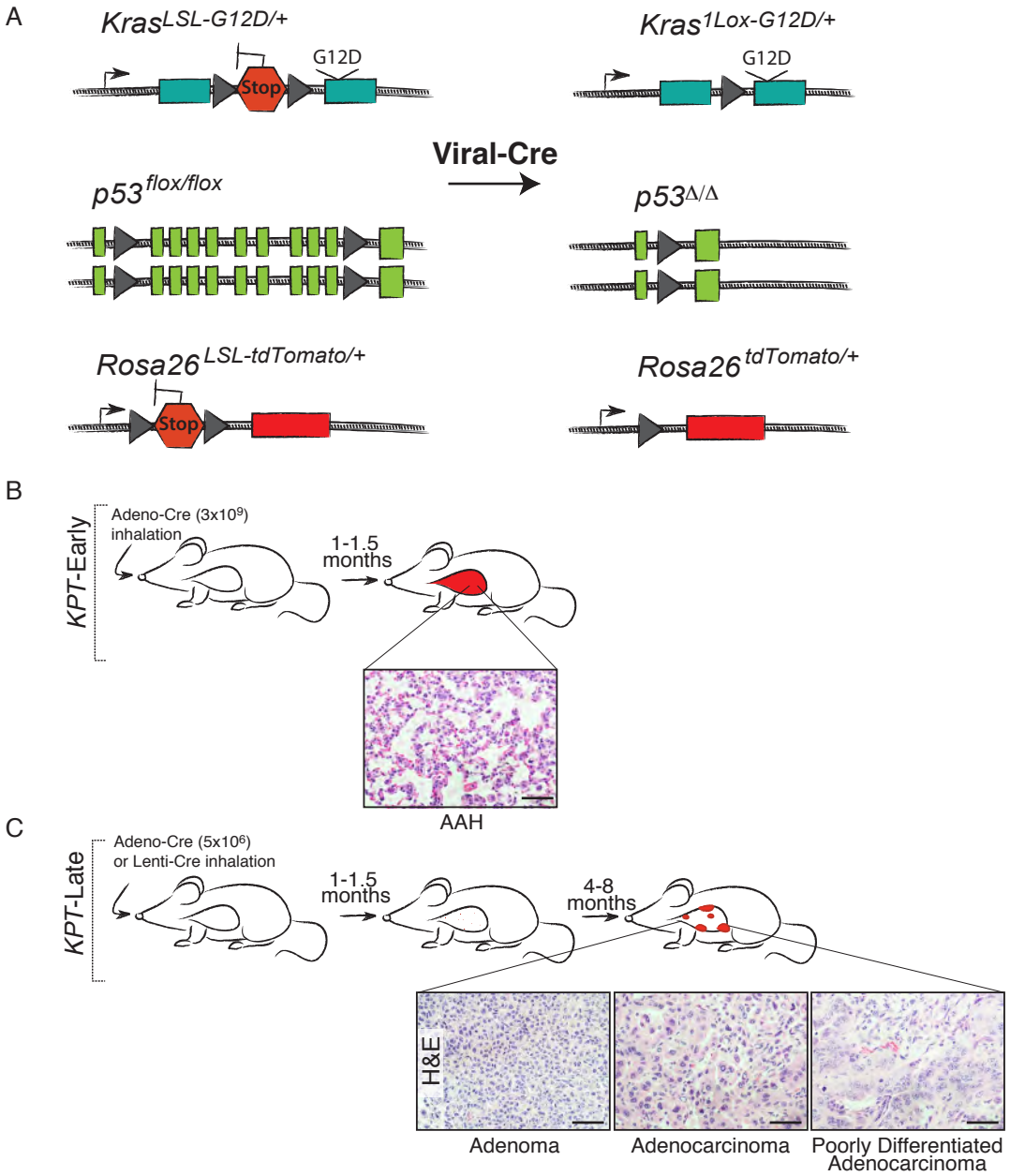

Supplemental Figure 1. Titratable induction of early and late stage lung cancer in *Kras*$^{LSLG12D/+}$;*p53*$^{flox/flox}$;*R26*$^{tdTomato/+}$ (*KPT*) mice

The accurate comparison of the dissemination ability of early and late stage lung cancer cells requires sophisticated modeling techniques. Monitoring an individual mouse over time is complicated by that fact that at early time points the number of hyperplastic cells is very small and as the tumors grow they both increase in cell number and evolve towards more advanced histological stages. If DTCs were detected only at the late time point it would remain unclear whether this reflects a gain in the phenotypic ability to disseminate or simply reflects the higher number of cancer cells at the later time points.To overcome this limitation we have used a system that allows the number of tumors lesions to be controlled by the viral-Cre titer.

A. The *Rosa26* knock-in Cre-reporter allele incorporated into the *Kras*$^{LSL-G12D}$;*p53*$^{flox/flox}$ lung adenocarcinoma mouse model.

B. *KPT*-Early mice (with tumors induced with 3x10^9 Adeno-Cre) have expansive atypical adenomatous hyperplasias (AAHs) with homogeneous cytological features, low nuclear to cytoplasmic ratio, and cells growing along the alveolar structure. Scale bar = 50 μM

C. *KPT*-Late mice (with tumors induced with 5x10^6 Adeno-Cre or Lenti-Cre) contain tumors at diverse stages including adenomas, adenocarcinomas and poorly differentiated adenocarcinomas all growing within large areas of normal lung. Adenomas have typical cytological features including low nuclear to cytoplasmic ratio with minimal cellular and nuclear pleiomorphism. Adenocarcinomas characteristically contain tumor giant cells and have high nuclear to cytoplasmic ratio. Some papillary structures can still be detected within areas of solid tumor growth. Poorly differentiated adenocarcinomas are distinguished by their characteristic invasiveness loss of all differentiated structure and robust stromal response. Scale bar = 50 μM