Supplementary Figure Legends

Supplementary Figure 1: Immunohistochemical analysis of *MYC*-induced adenocarcinoma. Proteins expressed in pulmonary epithelial cells were examined in the lungs of STM mice fed a DOX-free diet **(A, D, G)**, STM adenocarcinoma **(B, E, H)** and CTM adenocarcinoma **(C, F, I)**. **(A-C)** TTF-1 stained sections (brown stain with hematoxylin counter-stain). **(A)** Clara cells of the bronchiolar epithelium and type II pneumocytes in the alveolar space were TTF-1^+. Nuclear staining was also found in *MYC*-induced adenocarcinomas **(B, C)**. **(D-F)** SPC stained sections (red stain with Methyl Green counter-stain). Type II pneumocytes of the untreated lung **(D)** and lung adenocarcinomas from both STM **(E)** and CTM **(F)** mice were SPC^+. **(G-I)** CCSP stained sections (brown stain with hematoxylin counter-stain). Clara cells of the bronchiolar epithelium were $CCSP^+$ **(G)**, but adenocarcinomas from both STM **(H)** and CTM **(I)** mice were $CCSP^-$ (bar in **A** equals 0.1mm; **A-I** same magnification).

Supplementary Figure 2: *MYC* transgenic tumors have high RAS activity. A RAS activity assay was performed on protein lysates from STM and CTM lung adenocarcinomas (marked T) and adjacent normal lungs (marked L). High levels of activated RAS were found in tumor lysates. Western analysis showed that total levels of RAS protein were similar in normal lung and tumor tissues. β-ACTIN served as a loading control.

Supplementary Figure 3: Tumorigenesis in STM mice transduced with retrovirus expressing mutant RAS proceeds following removal of DOX. **(A)** Lungs from an STM mouse transduced with pMig-*HRAS*^{G12V} and continuously fed a DOX diet for 6 months. **(B)** Lungs from an STM mouse transduced with pMig-*HRAS*^{G12V} and fed a DOX diet for 1 month and then a DOX-free diet for 4 months (bars = 1mm).

Supplementary Figure 4: Adenocarcinomas that form after transduction of STM mice with *Kras*^{G12V} or *Kras*^{G12V}/*Mcl1* retrovirus over-express MYC protein and have hyperactive RAS. **(A, B)** H&E stained sections of STM mouse lungs transduced with *Kras*^{G12V}-expressing retrovirus **(A)** or retrovirus expressing both *Kras*^{G12V} and *Mcl1* **(B)**. Both were fed a DOX-free diet after transduction (bar in **A** and **B** equals 1mm). **(C)** Kaplan-Meier plot comparing the survival of mice fed diet free of DOX following transduction with retrovirus encoding *Kras*^{G12V} alone or both *Kras*^{G12V} and *Mcl1* together (Logrank, *p=0.1134*). **(D)** Western analysis of MYC and MCL1 in tumors from DOX-fed STM mice transduced with retrovirus encoding *Kras*^{G12V} or *Kras*^{G12V} together with *Mcl1*. **(E)** RAS activity assay on the same lysates as in **(D)**.

Supplementary Figure 5: Immunohistochemical analysis of tumors induced in STM mice by retroviral expression of mutant *RAS* alone or in combination with *Mcl1*. Tumors from STM mice transduced with activated RAS had a papillary growth pattern (H&E) **(A)** were TTF-1^+ **(B)**, SPC^+ **(C)** and $CCSP^-$ **(D)**, irrespective of DOX treatment. Tumors from DOX fed STM mice transduced with *Kras*^{G12V}/*Mcl1* retrovirus had a mixed morphology of papillary adenocarcinoma interspersed with areas of large cell undifferentiated carcinoma (H&E) **(E)**. Regions of large cell morphology were TTF-1^-

(F), SPC$^-$ **(G)** and CCSP$^-$ **(H)** (P in **E** and **F** marks papillary region and LC marks large cell undifferentiated carcinoma; bar in **A** equals 0.1mm; **A-H** same magnification).

Supplementary Figure 6: MCL1 and MYC expression in human NSCLC. Representative immunohistochemically stained cores are from a human lung tumor-tissue array. The antibody directed against MCL1 stained resident macrophages of normal lung tissue. MYC expressing cells were rare in normal lung tissues. Lung adenocarcinomas are shown that express different combinations of low and high MCL1 and MYC protein.