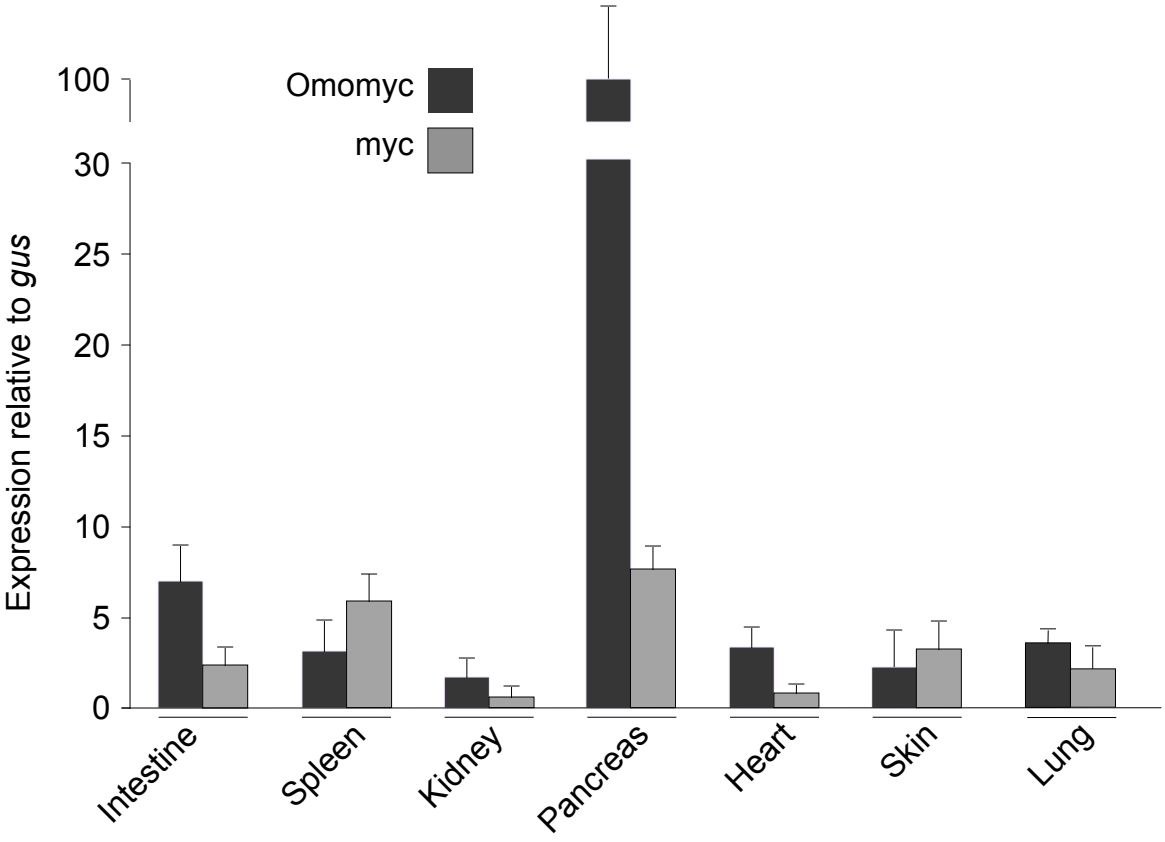
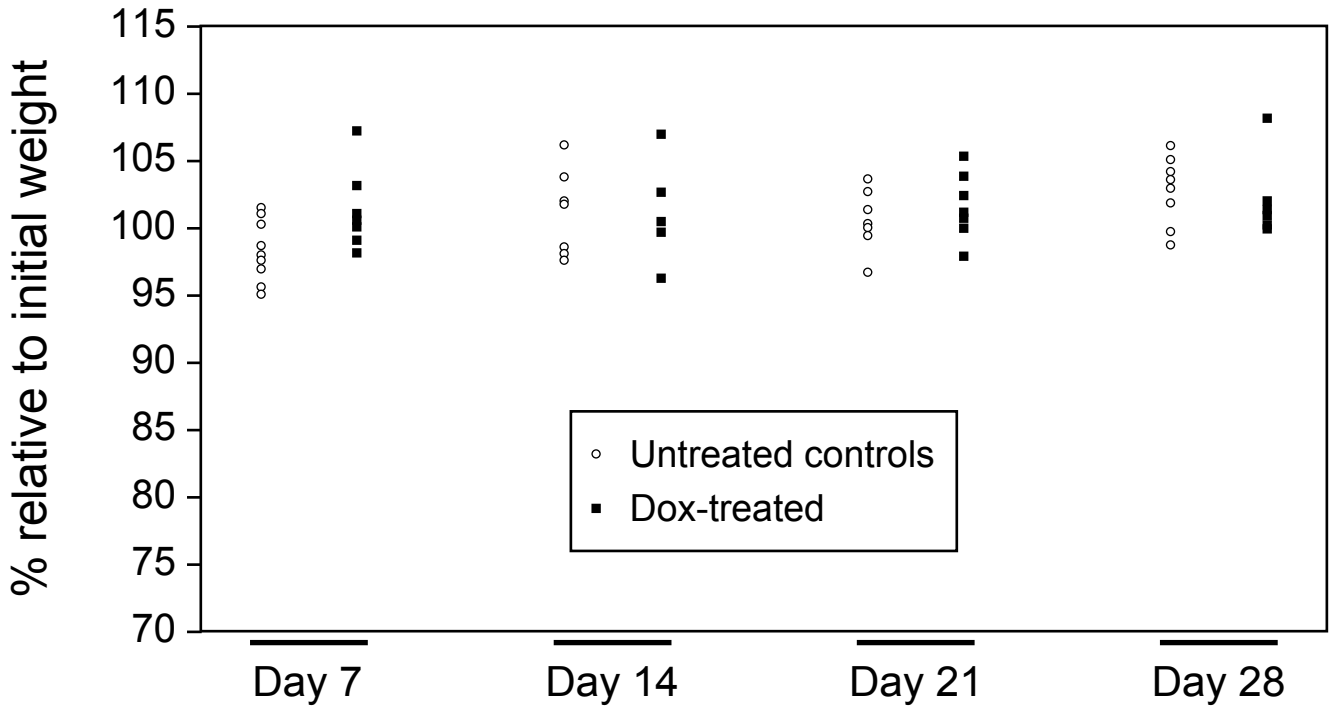
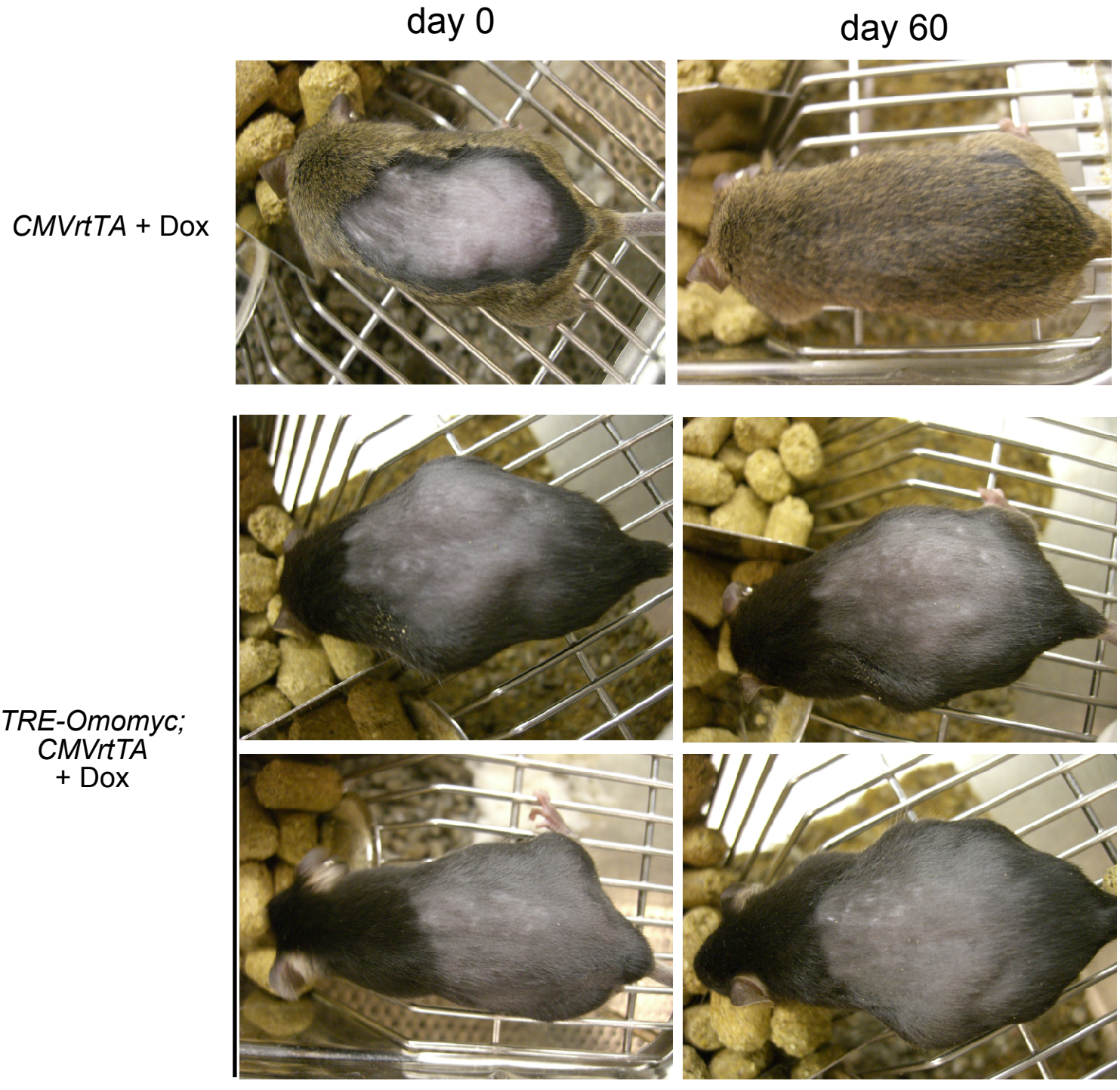
Supplementary Figure 1 Quantitation of Omomyc and c-Myc expression in mouse tissues. Real-time PCR of Omomyc and c-myc expression relative to GUS in various mouse tissues confirms widespread expression of the transgene at levels comparable or higher than c-myc.



Supplementary Figure 2. Influence of long-term systemic Omomyc expression on mouse weight. Graphical representation of weights of 4 week Doxycyclin treated animals versus untreated controls (cohorts of 8 mice each). Body weights are expressed as percentages of initial weight.

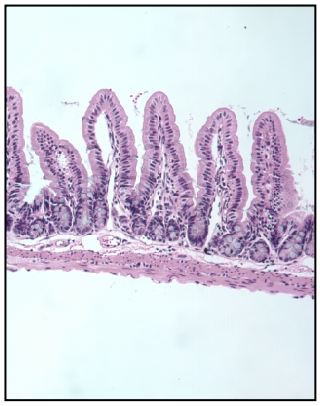


Supplementary Figure 3. Systemic Omomyc expression suppresses hair re-growth. Omomyc expressing mice (TRE-Omomyc;CMVrtTA+ Dox) and CMVrtTA-only expressing controls (CMVrtTA+ Dox) were shaved and subjected to Doxycyclin treatment for 2 months. Omomyc expression completely blocks hair re-growth.

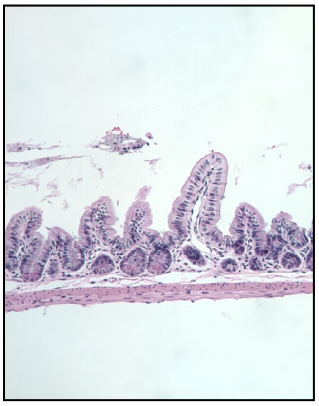


Supplementary Figure 4. Induction of Omomyc in TRE-Omomyc; -actin-rtTA mice recapitulates the intestinal and skin phenotypes of Doxycylin treated TRE-Omomyc;CMVrtTA mice and, additionally, elicits increased extramedullary hematopoiesis in spleen.
(a) H&E staining of small intestine (top panels) from -actin-rtTA or TRE-Omomyc; -actin-rtTA mice treated for 2 weeks with Doxycyclin.
(b) H&E staining of skin from -actin-rtTA or TRE-Omomyc; -actin-rtTA mice treated for 2 weeks with Doxycyclin.
(c) H&E-stained sections from spleen of control (-actin-rtTA) or Omomyc-expressing (TRE-Omomyc; -actin-rtTA) mice treated for 2 weeks with Doxycyclin.

a

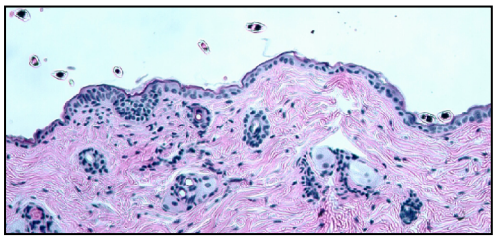


β-*actin-rtTA*
+ dox

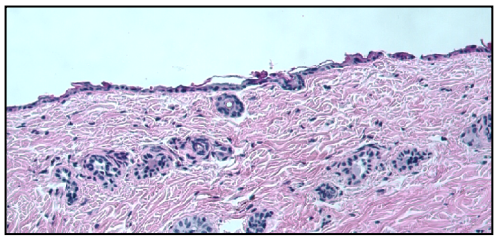


*TRE-Omomyc;*β-*actin-rtTA*
+ dox

b

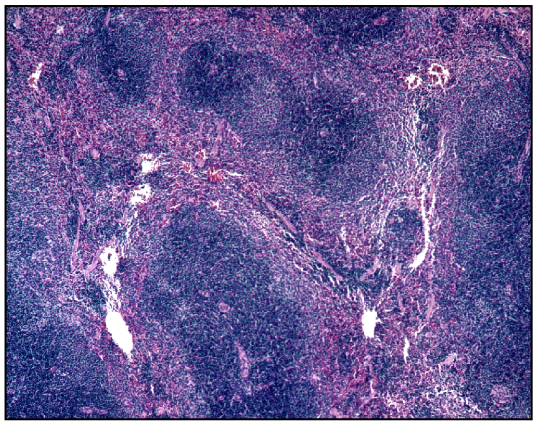


β-*actin-rtTA*
+ dox

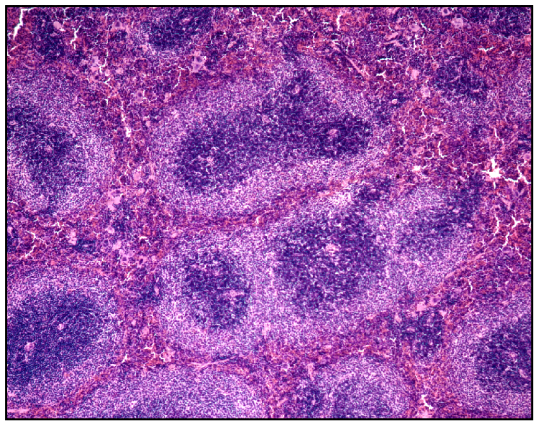


*TRE-Omomyc;*β-*actin-rtTA*
+ dox

c



β-*actin-rtTA*
+ dox



*TRE-Omomyc;*β-*actin-rtTA*
+ dox

Supplementary Table1. Long-term systemic Omomyc expression has no significant impact on blood chemistry (4 week Doxycyclin treated mice)

	Omomyc-expressing	Control
Alk. Phosphatase (U/L)	32.3 ± 17.5	32.6 ± 22.1
ALT (SGPT) (U/L)	66.6 ± 8.9	70.0 ± 16.9
Albumin (g/dL)	3.3 ± 0.1	3.4 ± 0.4
Total Protein (g/dL)	6.1 ± 0.05	6.1 ± 0.5
Globulin (g/dL)	2.8 ± 0.05	2.7 ± 0.1
Tot. Bilirubin (mg/dL)	0.1 ± 0.05	0.1 ± 0.05
Direct Bilirubin (mg/dL)	0.1 ± 0.05	0.1 ± 0.05
BUN (mg/dL)	26.6 ± 2.5	25.3 ± 0.5
Creatinin (mg/dL)	0.3 ± 0.1	0.3 ± 0.1
Calcium (mg/dL)	10.5 ± 0.05	10.3 ± 1.1
Phosphorus (mg/dL)	12.2 ± 0.6	13.0 ± 1.9
TCO_2 (mEq/L)	15.0 ± 1.0	12.3 ± 20.8
Chloride (mEq/L)	108.6 ± 1.5	108.0 ± 0.1
Potassium (mEq/L)	13.0 ± 0.6	15.1 ± 5.1
Sodium (mEq/L)	145.5 ± 0.5	142.0 ± 9.8
A/G ratio	1.1 ± 0.05	1.3 ± 0.1
B/C ration	88.9 ± 8.4	91.9 ± 34.5

Soucek et al. Supplementary Table 2

Myc inhibition causes anemia, which is rapidly resolved

Bone marrow studies: 1 week treatment

Control mice (expressing TREOmomyc or actin-rtTA only)		Omomyc mice (TREOmomyc;actin-rtTA+ Dox)		
Leukocytes:	Results	Leukocytes:	Results	Normal Range
WBC (K/ul)	5.94 ± 2.3	WBC (K/ul)	2.0 ± 1.1	1.8 - 10.7
NE (K/ul)	0.99 ± 0.6	NE (K/ul)	0.14 ± 0.3	0.1 - 2.4
LY (K/ul)	4.57 ± 3.1	LY (K/ul)	1.75 ± 0.7	0.9 - 9.3
MO (K/ul)	0.24 ± 0.1	MO (K/ul)	0.1 ± 0.1	0.0 - 0.4
EO (K/ul)	0.11 ± 0.02	EO (K/ul)	0.03 ± 0.01	0.0 - 0.2
BA (K/ul)	0.02 ± 0.01	BA (K/ul)	0.01 ± 0.01	0.0 - 0.2
NE (%)	17.11 ± 2.7	NE (%)	8.23 ± 5.2	6.6 - 38.9
LY (%)	76.19 ± 5.9	LY (%)	84.42 ± 9.8	55.8 - 91.6
MO (%)	4.49 ± 2.2	MO (%)	4.86 ± 1.2	0.0 - 7.5
EO (%)	1.9 ± 0.8	EO (%)	1.9 ± 1.5	0.0 - 3.9
BA (%)	0.3 ± 0.2	BA (%)	0.5 ± 0.6	0.0 - 2.0
Erythrocytes:		Erythrocytes:		
RBC (M/ul)	7.61 ± 1.1	RBC (M/ul)	2.33 ± 1.0	6.36 - 9.42
Hb (g/dl)	12.5 ± 1.2	Hb (g/dl)	3.3 ± 0.9	11.0 - 15.1
HCT (%)	39.3 ± 4.3	HCT (%)	12.2 ± 2.3	35.1 - 45.4
MCV (fL)	51.6 ± 1.6	MCV (fL)	53.3 ± 7.2	45.4 - 60.3
MCH (pg)	16.4 ± 2.0	MCH (pg)	14.3 ± 1.3	14.1 -19.3
MCHC (g/dl)	31.8 ± 0.9	MCHC (g/dl)	26.8 ± 2.0	30.2 - 34.2
RDW (%)	18.0 ± 2.1	RDW (%)	18.3 ± 1.8	12.4 - 27.0
Thrombocytes		Thrombocytes		
PLT (K/ul)	277 ± 131	PLT (K/ul)	77 ± 69	592 - 2972
MPV (fL)	6.1 ± 1.1	MPV (fL)	6.1 ± 0.9	5.0 - 20.0

Bone marrow studies: 2 week treatment

Control mice (expressing TREOmomyc or actin-rtTA only)		Omomyc mice (TREOmomyc;actin-rtTA+ Dox)		
Leukocytes:	Results	Leukocytes:	Results	Normal Range
WBC (K/ul)	2.03 ± 0.3	WBC (K/ul)	4.7 ± 2.2	1.8 - 10.7
NE (K/ul)	0.44 ± 0.2	NE (K/ul)	0.87 ± 0.8	0.1 - 2.4
LY (K/ul)	1.43 ± 0.3	LY (K/ul)	2.7 ± 0.3	0.9 - 9.3
MO (K/ul)	0.1 ± 0.1	MO (K/ul)	0.19 ± 0.1	0.0 - 0.4
EO (K/ul)	0.04 ± 0.02	EO (K/ul)	0.05 ± 0.03	0.0 - 0.2
BA (K/ul)	0.02 ± 0.01	BA (K/ul)	0.03 ± 0.01	0.0 - 0.2
NE (%)	21.88 ± 5.3	NE (%)	34.9 ± 3.2	6.6 - 38.9
LY (%)	70.4 ± 4.2	LY (%)	59.02 ± 3.3	55.8 - 91.6
MO (%)	5.12 ± 0.6	MO (%)	4.11 ± 1.0	0.0 - 7.5
EO (%)	1.85 ± 1.0	EO (%)	1.18 ± 0.9	0.0 - 3.9
BA (%)	0.74 ± 0.2	BA (%)	0.7 ± 0.4	0.0 - 2.0
Erythrocytes:		Erythrocytes:		
RBC (M/ul)	7.61 ± 1.1	RBC (M/ul)	10.76 ± 1.2	6.36 - 9.42
Hb (g/dl)	12.5 ± 1.2	Hb (g/dl)	14.25 ± 0.9	11.0 - 15.1
HCT (%)	39.3 ± 4.3	HCT (%)	48.6 ± 2.0	35.1 - 45.4
MCV (fL)	51.6 ± 1.6	MCV (fL)	49.85 ± 2.2	45.4 - 60.3
MCH (pg)	16.4 ± 2.0	MCH (pg)	14.6 ± 0.7	14.1 -19.3
MCHC (g/dl)	31.8 ± 0.9	MCHC (g/dl)	29.35 ± 1.8	30.2 - 34.2
RDW (%)	18.0 ± 2.1	RDW (%)	16.95 ± 1.7	12.4 - 27.0
Thrombocytes		Thrombocytes		
PLT (K/ul)	277 ± 131	PLT (K/ul)	276 ± 110	592 - 2972
MPV (fL)	6.1 ± 1.1	MPV (fL)	5.8 ± 0.4	5.0 - 20.0

Soucek et al. Supplementary Table 3

Summary of number and genotypes of mice used for each experiment

GENOTYPE	# mice
Prevention study in LSL-Kras driven lung tumors: 4 week treatment	
TRE-Omomyc;CMV-rtTA;LSLKRas +Dox	5
LSLRas +Dox	4
TRE-Omomyc +Dox	4
TRE-Omomyc;CMV-rtTA;LSLKRas -Dox	3
LSLKRas -Dox	4
CMV-rtTA -Dox	4
Intervention study in LSL-Kras driven lung tumors: 6 weeks + 1 week treatment	
TRE-Omomyc;CMV-rtTA;LSLKRas +Dox	4
CMV-rtTA;LSLRas +Dox	3
TRE-Omomyc +Dox	3
TRE-Omomyc;CMV-rtTA;LSLKRas -Dox	3
TRE-Omomyc;LSLKRas -Dox	3
TREOmomyc;CMVrtTA -Dox	3
Intervention study in LSL-Kras driven lung tumors: 18 weeks + 4 week treatment	
TRE-Omomyc;CMV-rtTA;LSLKRas +Dox	6
CMV-rtTA;LSLRas +Dox	3
TREOmomyc;LSLRas +Dox	3
TRE-Omomyc +Dox	3
TRE-Omomyc;CMV-rtTA;LSLKRas -Dox	3
LSLKRas -Dox	3
TREOmomyc;CMVrtTA -Dox	3
Side effects studies: 4 week treatment	
TREOmomyc;CMVrtTA + Dox	8
TREOmomyc + Dox	7
CMV-rtTA -Dox	8
TREOmomyc;CMVrtTA - Dox	6
TREOmomyc - Dox	4
CMV-rtTA +Dox	6
Blood counts: 1 week treatment	
TREOmomyc;actin-rtTA + Dox	3
TREOmomyc + Dox	2
actin-rtTA +Dox	2
TREOmomyc;actin-rtTA - Dox	2
TREOmomyc - Dox	2
actin-rtTA -Dox	1
Blood counts: 2 week treatment	
TREOmomyc;actin-rtTA + Dox	6
TREOmomyc + Dox	2
actin-rtTA +Dox	2
TREOmomyc;actin-rtTA - Dox	3
TREOmomyc - Dox	2
actin-rtTA -Dox	2