

Supporting Information

Inhibition of Endotrophin, a Cleavage Product of Collagen VI, Confers Cisplatin Sensitivity to Tumors

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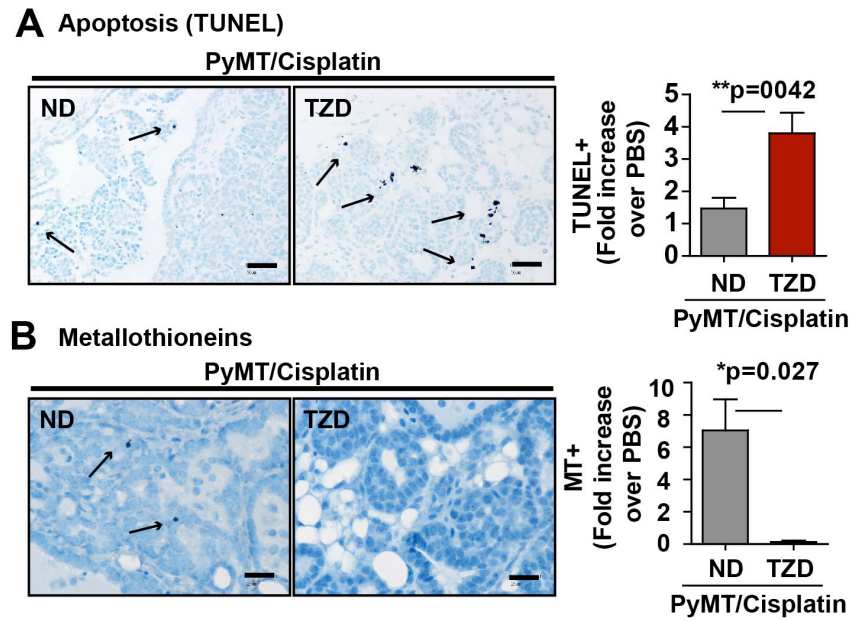


Fig. S1. TZD confers beneficial effects on cisplatin treatment in mammary tumors. Met-1 cancer cells (0.5×10^6 cells/ mouse) were implanted into wild-type mice and TZD (20 mg/ kg) was given by diet and cisplatin (1 mg/ kg) was intraperitoneally (ip.) injected every 5 days from 30 days post implantation (n=8/ group). *** $p < 0.001$ vs. ND by 2-way ANOVA. Tumor tissues from PyMT mice given TZD or normal diet (ND) diet were histologically assessed. Representative images and quantification for TUNEL staining (A), showing increased cancer cell apoptosis by TZD combination in cisplatin. Data represent mean \pm SD (n=5/ group). ** $p = 0.0042$ ND vs. TZD by *unpaired student t-test*. Scales: 50 μ m. Representative metallothioneins staining and quantification (C), showing a higher signal in tumor tissues following cisplatin, which is efficiently suppressed by TZD combination. Data represent mean \pm SD (n=5/ group). * $p = 0.002$ ND vs. TZD by *unpaired student t-test*. Arrows indicate staining positive cells. Scales: 25 μ m.

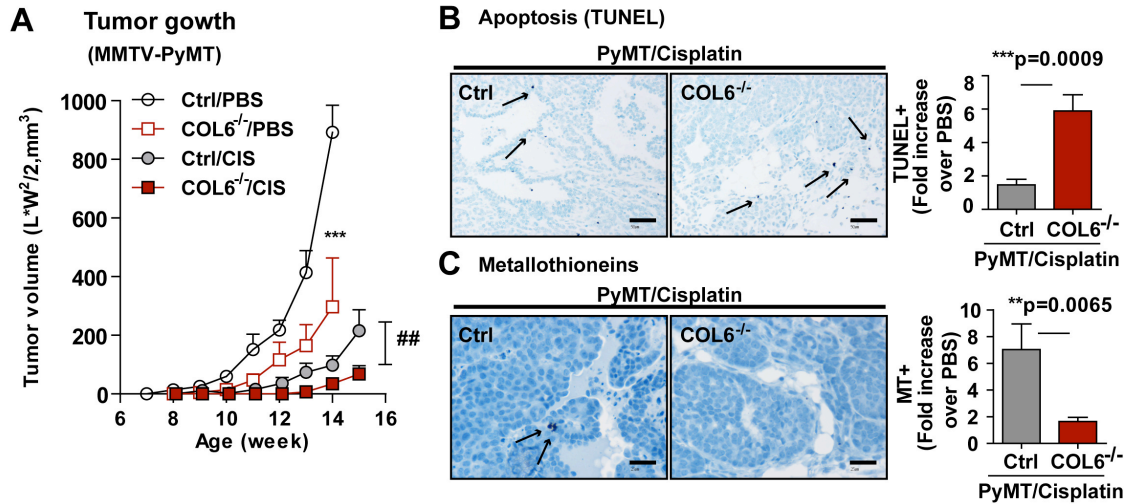


Fig. S2. The absence of COL6 sensitizes tumors to cisplatin treatment. **A.** 10-weeks aged PyMT and PyMT/COL6^{-/-} mice were given cisplatin (1 mg/kg, ip., 2 times/ week) over tumor progression. Tumor growth was determined by caliper measurements. Data represent mean \pm SD (n=8/ group). ***p<0.001 Ctrl/PBS vs. COL6^{-/-}/PBS; ##p<0.01 Ctrl/CIS vs. COL6^{-/-}/CIS by 2-way ANOVA. **B.** Representative TUNEL staining images and quantification, showing significantly increased cancer cell apoptosis in PyMT/COL6^{-/-} mice by cisplatin treatment. Data represent mean \pm SD (multiple images from n=5/ group). ***p<0.0009 Ctrl vs. COL6^{-/-} by unpaired student t-test. Scales: 50 μ m. **C.** Representative metallothioneins staining and quantification, showing a higher signal in tumor tissues following cisplatin which is efficiently suppressed in COL6^{-/-} mice. Data represent mean \pm SD (n=5/ group). **p<0.0065 Ctrl vs. COL6^{-/-} by unpaired student t-test. Arrows indicate staining positive cells. Scales: 25 μ m.

Table S1. Primer sequences used for qRT-PCR

Gene	Sense	Antisense
Snail (Snai1)	CCCTTCAGGCCACCTTCTTTGAGGT	GTCCAGTAACCACCCTGCTG
Slug (Snai2)	CTGTATGGACATCGTCGGCAG	ACTTACACGCCCCAAGGATG
Twist1	CGGCCAGGTACATCGACTTC	TGCAGCTTGCCATCTTGGAG
Twist2	TCAGCAAGATCCAGACGCTC	CTGAGATGTGCAGGTGGGTC
E-Cadherin (Cdh1)	CGATTACGAGGGCAGTGGTT	AGTCCCCTAGTCGTCCTCAC
N-Cadherin (Cdh2)	GGCAATCCCACCTTATGGCCT	TCCGTGACAGTTAGGTTGGC
Vimentin	GCCAGCAGTATGAAAGCGTG	ACCTGTCTCCGGTACTCGTT
S100A4	TTGTGTCCACCTTCCACAAA	TGTTGCTGTCCAAGTTGCTC
COL6A3-N	ACGCCCATCACC ACTCTAAC	CTAAACTGCACGACCCCAAT
36B4	GGCATGCGGCCCGTCTCTC	CTCCCTGGGCATCACGGCG