

Figure S1. Distribution of methionine adenosyltransferase 1a (*MAT1A*) expression in healthy human tissues and in bladder cancer. (A) RNA sequencing (RNA-seq) profiling *MAT1A* expression in normal human tissues, values obtained from Fagerberg et al. [10]. (B) Immunohistochemistry (IHC) of normal liver tissue obtained from The Human Protein Atlas, available from <http://www.proteinatlas.org>, positive for *MAT1A* expression [11]. (C) IHC of normal bladder tissue obtained from The Human Protein Atlas, available from <http://www.proteinatlas.org>, negative for *MAT1A* expression [11].

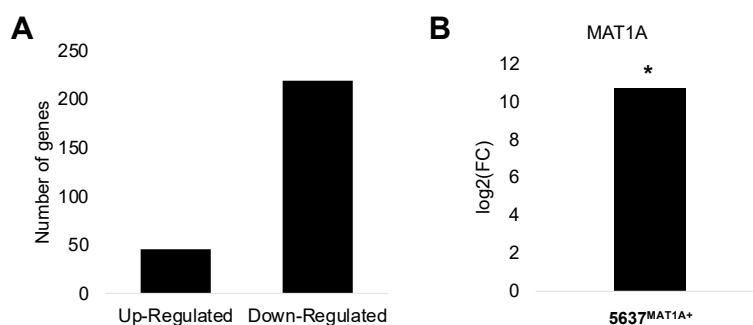


Figure S2. RNA-seq profiling of 5637^{MAT1A+} cells. (A) Total number of up- and down-regulated genes in 5637 cells overexpressing *MAT1A* (5637^{MAT1A+}) compared to empty vector transfected control cells (5637), n=3 biological replicates. (B) *MAT1A* gene expression expressed in log₂ fold change based on RNA sequencing data, FDR<0.05(*).

Table S1. Top 20 down-regulated genes in drug relapsed patient-derived bladder cancer xenograft (PDX) tumors.

Ranking	Gene Symbol	Gene Name	BL0293_FC	BL0440_FC
1	SNORD14C	Small Nucleolar RNA, C/D Box 14C	-3.26	-1.61
2	SNORD31	Small Nucleolar RNA, C/D Box 31	-2.53	-1.91
3	KRT15	Keratin 15	-2.43	-1.85
4	JMJD7- PLA2G4B	Jumonji Domain Containing 7-Phospholipase A2, Group IVB (Cytosolic) Read-Through	-2.64	-1.63
5	PITRM1-AS1	PITRM1 Antisense RNA 1	-2.46	-1.61
6	MLXIPL	MLX Interacting Protein Like	-2.10	-1.95
7	ANXA5	Annexin A5	-2.07	-1.80
8	SNORD29	Small Nucleolar RNA, C/D Box 29	-1.81	-2.04
9	LPIN3	Lipin 3	-2.16	-1.67
10	PDXDC2P	Pyridoxal Dependent Decarboxylase Domain Containing 2, Pseudogene	-2.21	-1.60
11	PRRT2	Proline Rich Transmembrane Protein 2	-1.86	-1.74
12	DDX12P	DEAD/H-Box Helicase 12, Pseudogene	-2.02	-1.53
13	GNRH1	Gonadotropin Releasing Hormone 1	-2.03	-1.51
14	C10orf55	Chromosome 10 Open Reading Frame 55	-1.82	-1.55
15	C11orf68	Chromosome 11 Open Reading Frame 68	-1.64	-1.73
16	NLRP1	NLR Family Pyrin Domain Containing 1	-1.74	-1.60
17	P2RX7	Purinergic Receptor P2X 7	-1.54	-1.51

Table S2. Patient characteristics. 55 patients' tissues were used in this study and their characteristics are described below. The patients were all diagnosed with bladder cancer and underwent radical cystectomy for the treatment of bladder cancer.

	N	55
Race	Caucasian	35 (63.64%)
	Asian	1 (1.82%)
	African American	1 (1.82%)
	Unknown	18 (32.73%)
Ethnicity	Hispanic/Latino	4 (7.27%)
	Not Hispanic/Latino	34 (61.82%)
	Unknown	17 (30.91%)
Age	Median	68 (36-85)
Gender	Male	45 (81.82%)
	Female	10 (18.18%)
Type	Transitional Cell Carcinoma	28 (50.91%)
	Urothelial Carcinoma	23 (41.82%)
	Papillary/Squamous Cell Carcinoma	4 (7.27%)
Grade	High Grade	23 (41.82%)
	Intermediate Grade	23 (41.82%)
	Low Grade	4 (7.27%)
	not reported/undetermined	5 (9.09%)
Neoadjuvant Treatment	BCG	4 (7.27%)
	Chemotherapy	11 (20.00%)
	None Reported	40 (72.73%)

Table S3. Top pathway ontologies downregulated in 5637^{MAT1A+} overexpressing cells identified using ToppGene.

Name	pValue
DNA Damage/Telomere Stress Induced Senescence	3.971e-17
Cellular Senescence	1.262e-15
Condensation of Prophase Chromosomes	8.061e-15

Senescence-Associated Secretory Phenotype (SASP)	1.307e-14
HDACs deacetylate histones	1.451e-14
RNA Polymerase I Promoter Opening	1.735e-14
Packaging of Telomere Ends	2.368e-14
DNA methylation	2.750e-14
Activated PKN1 stimulates transcription of AR (androgen receptor) regulated genes KLK2 and KLK3	4.290e-14
SIRT1 negatively regulates rRNA Expression	6.592e-14
