

Supplemental Table 1. IC₅₀ values of ganetespib on MCL cell lines JEKO-1, GRANTA-519, and MINO when treated either constantly for 72 h or transiently for 12h.

Cell lines	Ganetespib (IC ₅₀ , nM)	
	Constantly (72 h)	Transiently (12 h)
JEKO-1	13.9 ± 3.1	18.8 ± 2.9
GRANTA-519	47.7 ± 9.3	51.7 ± 7.1
MINO	67.4 ± 10.1	73.6 ± 11.0

Table S2. Genes changed in the same direction in three MCL cell lines.

HSP-related	DNA Replication and Cell Cycle	B-Cell Marker	Unknown
HSP90AA1	MCM4	HLA-DQA1	CHORDC1
HSPA1B	MCM7	HLA-DMB	DEDD2
BAG3	MCM8		CASP1
DNAJB1	CDC6		DLEU2
DNAJB4	CDC45		ZNF367
	RMI2		NUDT6
	PRIM1		TMEM106C
			TCF19
			ARL6IP6
			DTL

Note: red means up-regulation, blue indicates down-regulation.

Table S3. The transcription factor candidates.

TF candidate	Number of articles related	Number of targeting gene (predicted)
E2F1	39	6
p53	70	6
AR	10	2
c-Myc	32	4

Supplemental Table 4. IC₅₀ values of different cell lines with indicated treatment.

Cell lines	Everolimus (IC ₅₀ , nM)			Temsirolimus (IC ₅₀ , nM)		
	Vehicle	Ganetespib (30 nM)	<i>P</i> values	Vehicle	Ganetespib (45 nM)	<i>P</i> values
JEKO-1	108.2 ± 33.75	8.147 ± 4.461	0.042	2.755 ± 0.5928	1.286 ± 0.3135	0.094
GRANTA-519	5026 ± 1172	243.0 ± 48.17	0.015	2409 ± 430.6	374.4 ± 49.84	0.009

Note: the indicated cell lines were pre-treated with or without ganetespib for 12 hours, before they were treated with Everolimus or Temsirolimus. Data were presented as mean ± SD except for the increases of sensitivity.

Supplementary Table 5. Antibodies used in this study.

Primary antibody					
Targeted protein	Catalog No.	Source	Company	Application	Note
Akt	#2920	Mouse	Cell Signaling Technology	Western blot, 1:1000 Immunohistochemistry, 1:100	
STAT3	#9139	Mouse			
Cyclin D1	#2978	Rabbit			Immunohistochemistry, 1:50
NF-κB1	#3035	Rabbit			
p-Erk1/2(Thr202/Tyr204)	#9101	Rabbit			
phospho-Histone H2A.X(Ser139)	#2577	Rabbit			
Cdk1	ab126762	Rabbit			Abcam
BTK	ab208937	Rabbit			
c-Myc	ab32072	Rabbit			
CDC6	ab109315	Rabbit			
MCM4	ab124836	Rabbit			
MCM7	ab52489	Rabbit			
CDC45	ab126762	Rabbit			
HSP90	UMA50002	Mouse	General Biosystems		
Ki67	sc-23900	Mouse	Santa cruz Biotechnology		
E2F1	sc-251	Mouse			
ALK	sc-398791	Mouse			
Bcl-6	sc-7388	Mouse			

JAK1	sc-1677	Mouse	Ruiying Biological		
Cdk2	sc-6248	Mouse			
Cdk4	sc-23896	Mouse			
Cdk6	sc-7961	Mouse			
PRIM1	sc-390265	Mouse			
AR	sc-7305	Mouse			
Bcl-2	RLM3041	Mouse			
Survivin	RLM3419	Mouse			
Cyclin B	RLT1169	Rabbit			
Erk1/2	RLT1625	Rabbit			
HSP90	RLM3480	Mouse			
RMI2	PA5-59381	Rabbit	Thermo Fisher Scientific		
53BP1	A300-272A	Rabbit	BETHYL	Immunofluorescence, 1:1000	
β -actin	A1978	Mouse	Cell Signaling Technology		
Secondary antibody					
Goat anti-rabbit Alexa-fluor 488	A11008	Goat	Life Technologies	Immunofluorescence	1:1000
Goat anti-Mouse IgG(H+L)-HRP	115-035-003	Goat	Jackson ImmunoResearch	Western blot	1:5000
Goat anti-Rabbit IgG(H+L)-HRP	315-035-005	Goat	Jackson ImmunoResearch	Western blot	1:5000

Supplemental Table 6. siRNA sequences used in the experiments.

Target	Sequences (sense)	Sequences (anti-sense)
Scrambled	GUAGCCAUGAUUGACCAUATT	UAUGGUCAAUCAUGGCUACTT
siE2F1	GGGACUCUGUUGGGAACAUTT	AUGUCCCAACAGAGUCCCTT
HSP90-01	GGAAUUCAGAGCCCUUCUATT	UAGAAGGGCUCUGAAUUCCTT
HSP90-02	GAAUUCAGAGCCCUUCAUTT	AUAGAAGGGCUCUGAAUUCTT

Supplemental Table 7. Primers for qRT-PCR experiments.

Genes	Forward primer (5'-3')	Reverse Primer (5'-3')
GAPDH	CAAGGTCATCCATGACAACCTTG	GTCCACCACCCTGTTGCTGTAG
CDC6	TGGTGCTGATTGGTATTGCT	TTTGCGGGCACAGAATTGAA
CDC45	TAGGCCAGTCAATGTCGTCA	GAAGGCTCTGACCCATCACT
MCM4	G TTCACCACTGACATACGGC	AGACTGCTCACTTGCCACTA
MCM7	AGCCCATCGGATTGTGAAGA	CCGGATTTTCATGCCTCGAG
MCM8	ACCTTGAGCTCCGGAAACA	CATGCTGGGATCGCTCAAAA
PRIM1	AAGTGCTGGACCCTCATGAC	TTAACGTCTTGACCACCCTTT
RMI2	TGATGGTGATGGGAGTGTT	AGTGTCCATGAAATCCACATCA

Supplemental Figures

Supplemental Figure 1. HSP90 knockdown in GRANTA-519 and MINO cells.

Supplemental Figure 2. Protein levels of reported lymphoma-related HSP90 clients after 12-hour ganetespib treatment. Protein expression levels of Akt, ALK, BCL2, BCL6, JAK1, STAT3, BTK, Cdk1, Cdk2, Cdk4, Cdk6, Cyclin B, Cyclin D, Erk1/2, and c-Myc in cells with or without 12-hour ganetespib treatment. The time points chosen here are 0 and 12 hours post drug treatment.

Supplemental Figure 3. The results of pathway enrichment using Reactome Database for the regulated genes in JEKO-1 (A), GRANTA-519 (B), and MINO (C) cells with 12-hour ganetespib treatment.

Supplemental Figure 4. Pathway enrichment of the 24 genes identified in Figure 4D using Reactome Pathway Database.

Supplemental Figure 5. The mRNA levels of CDC6, CDC45, MCM4, MCM7, MCM8, PRIM1, and RMI2 in GRANTA-519 and MINO cells with or without 12-hour ganetespib treatment.

Supplemental Figure 6. The graphic abstract.

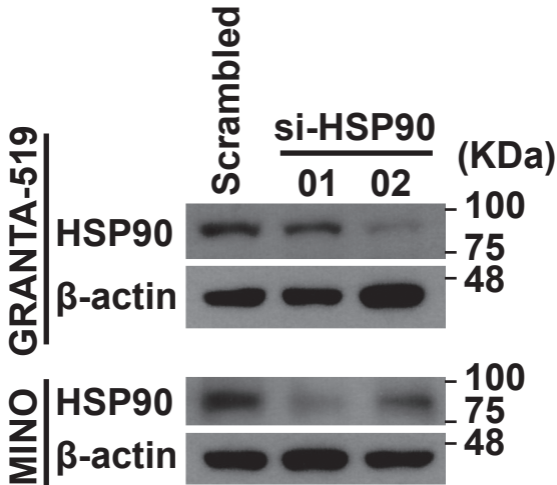


Figure S1

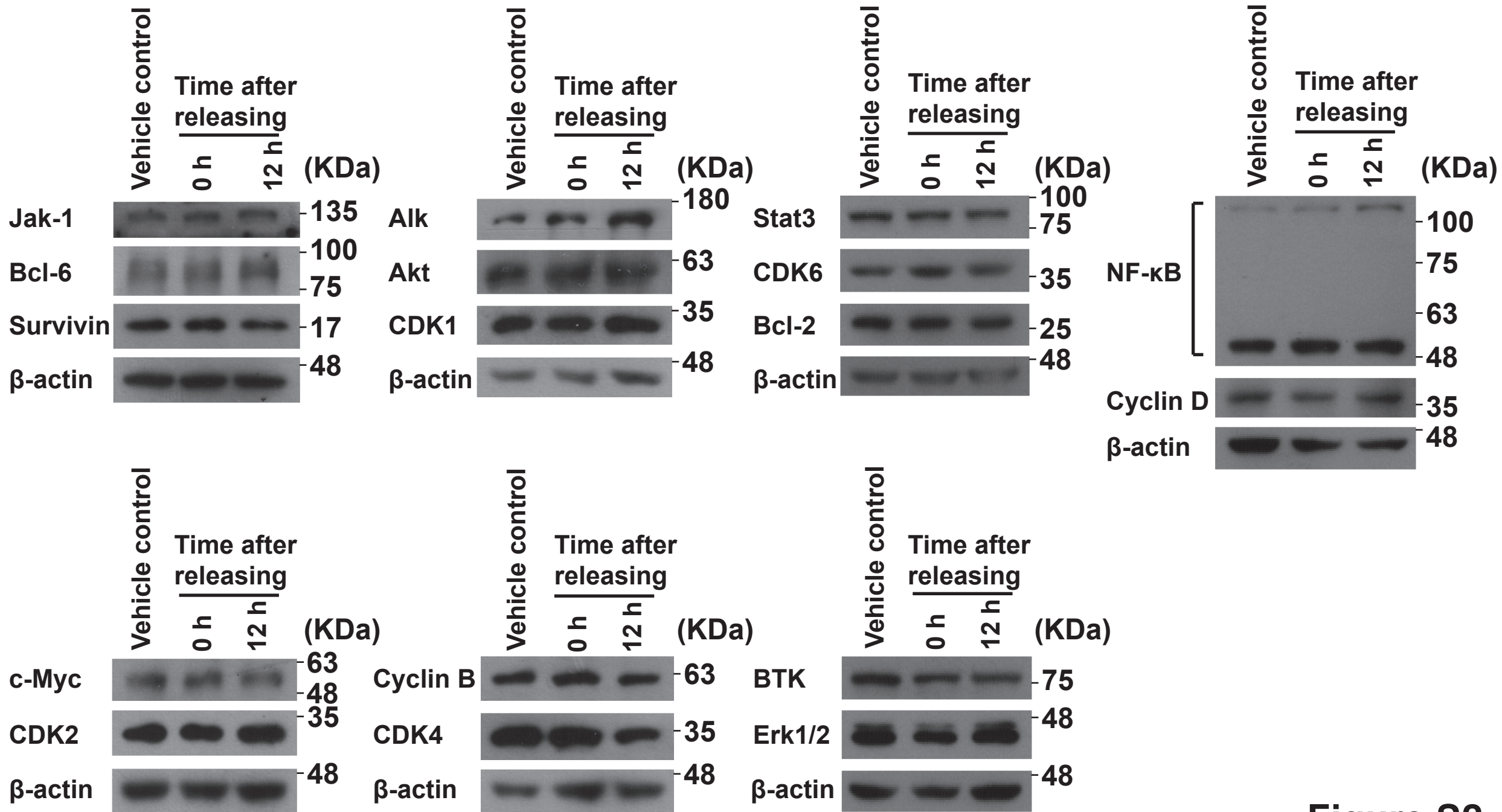
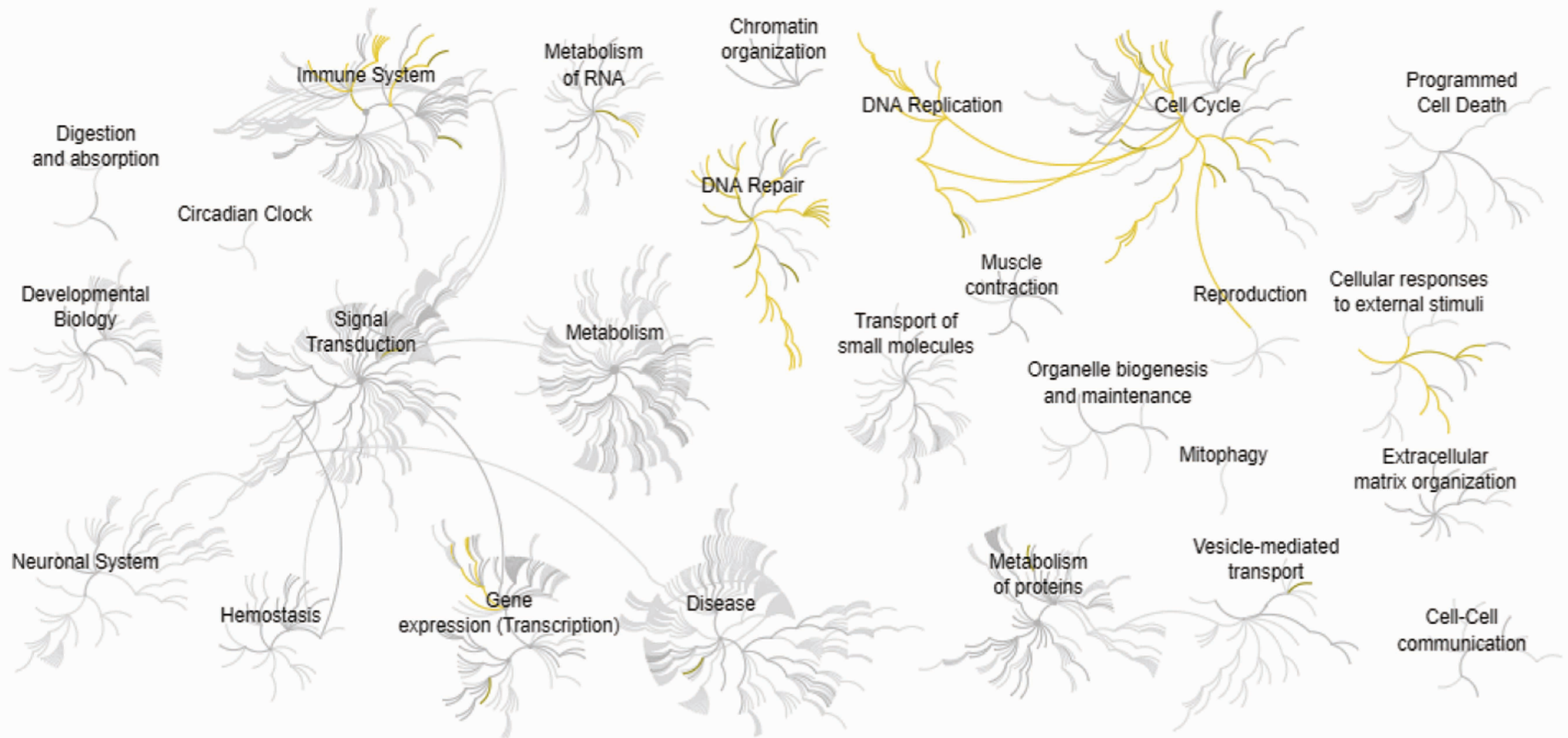
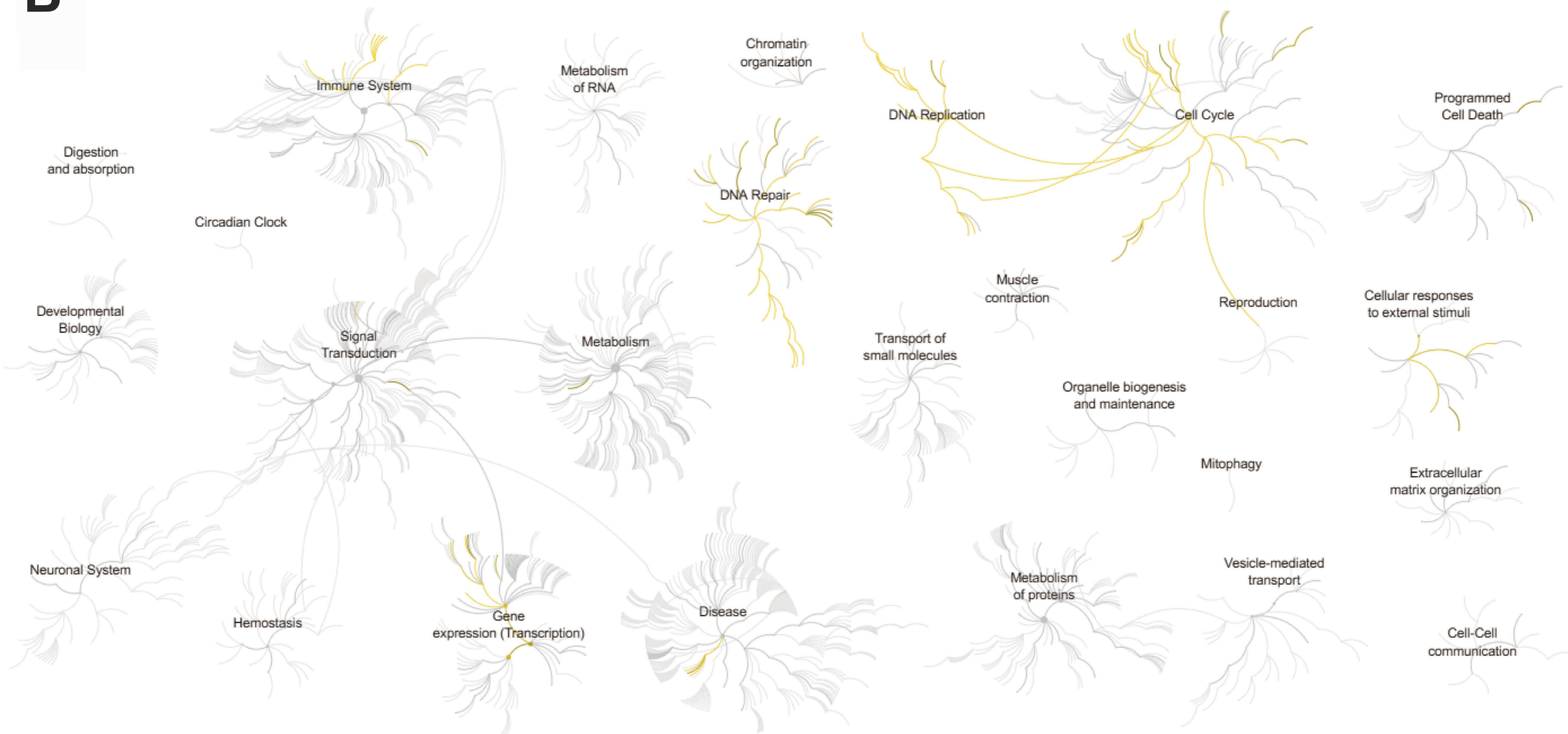
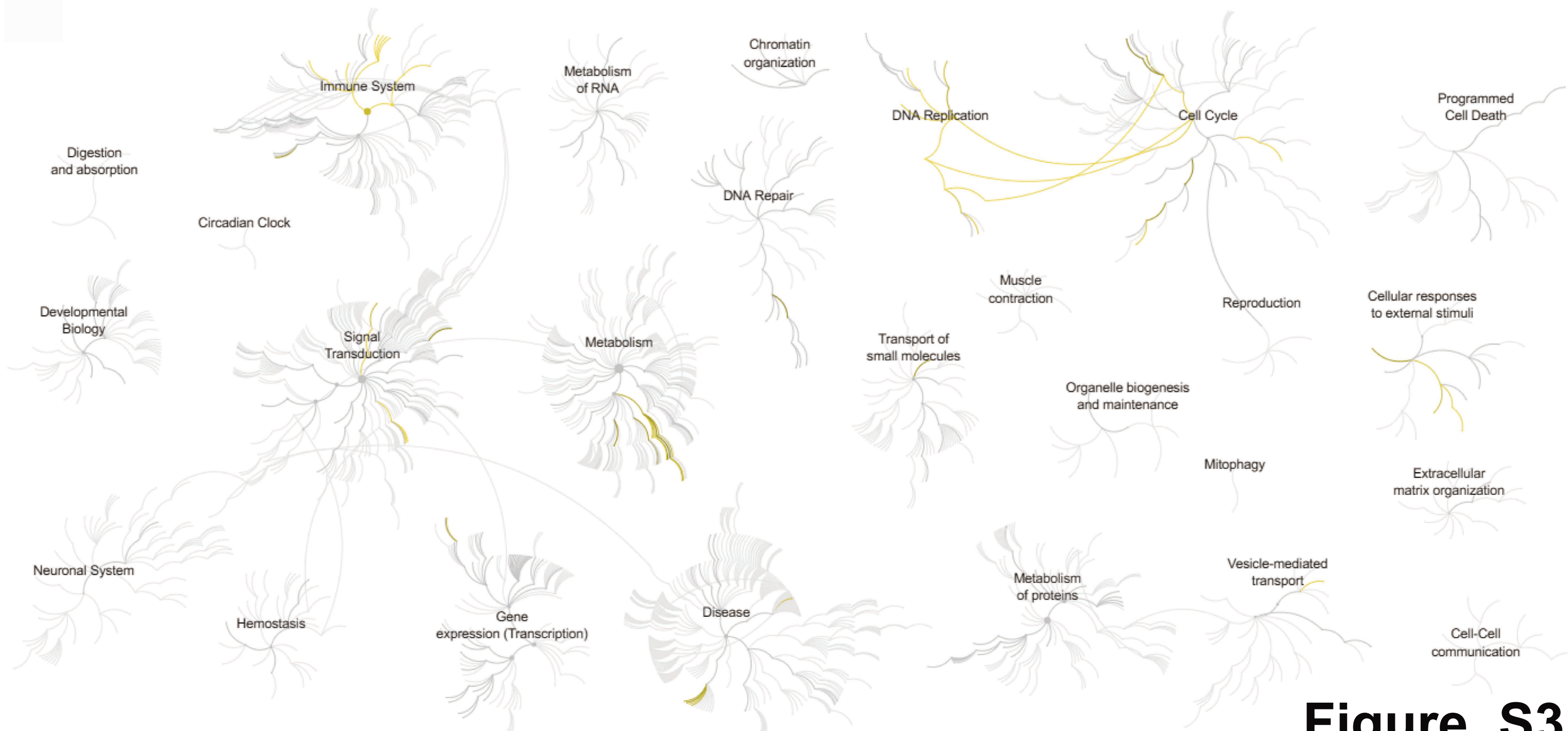


Figure S2

A**B****C****Figure S3**

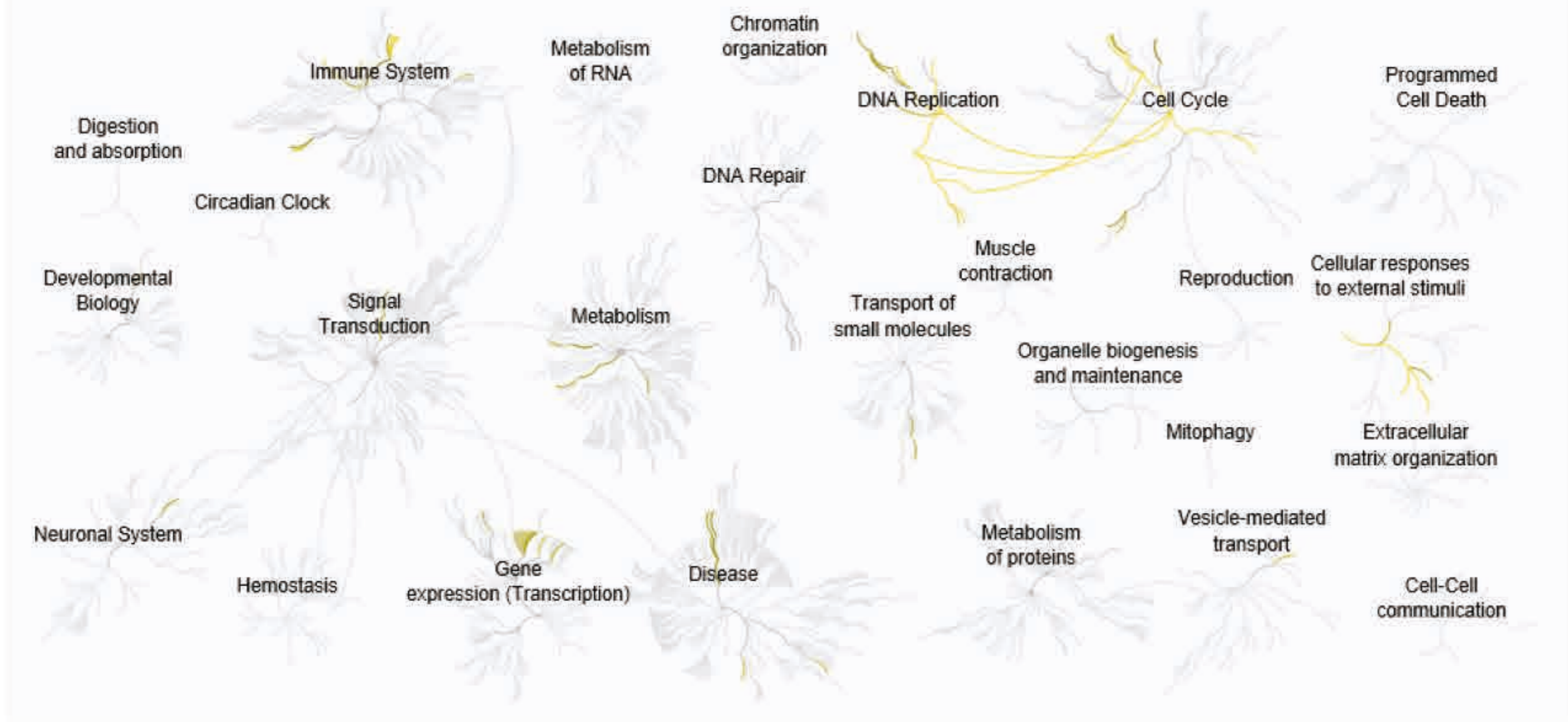


Figure S4

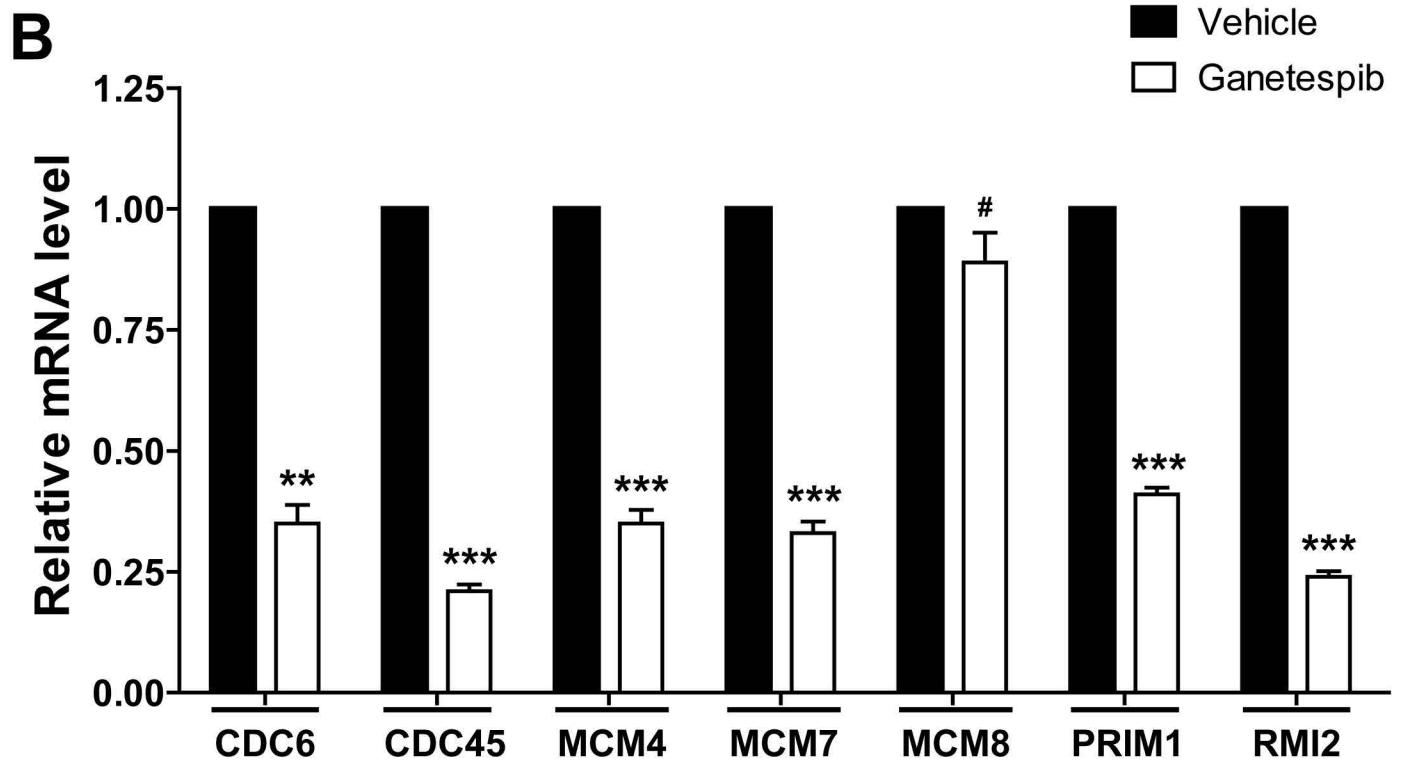
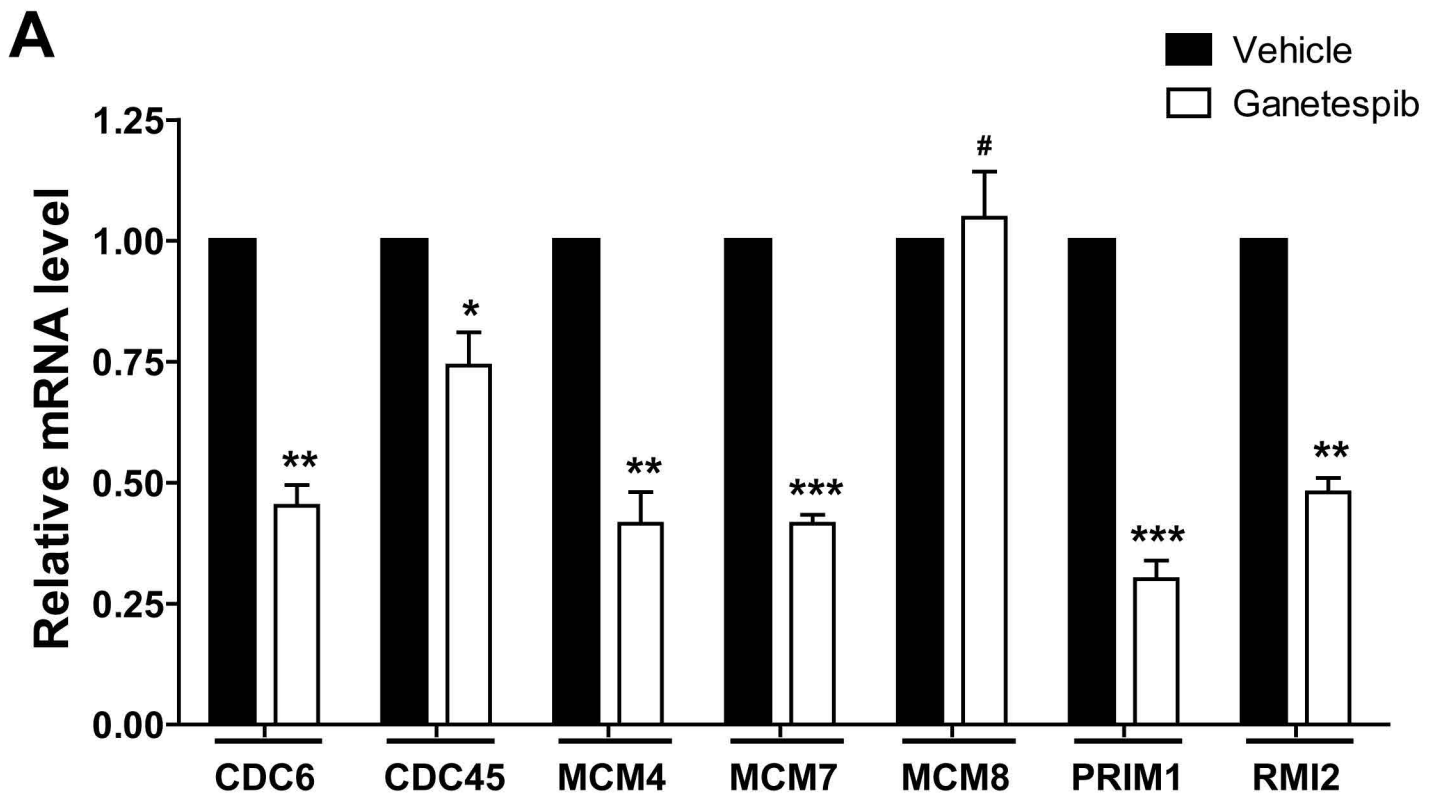


Figure S5

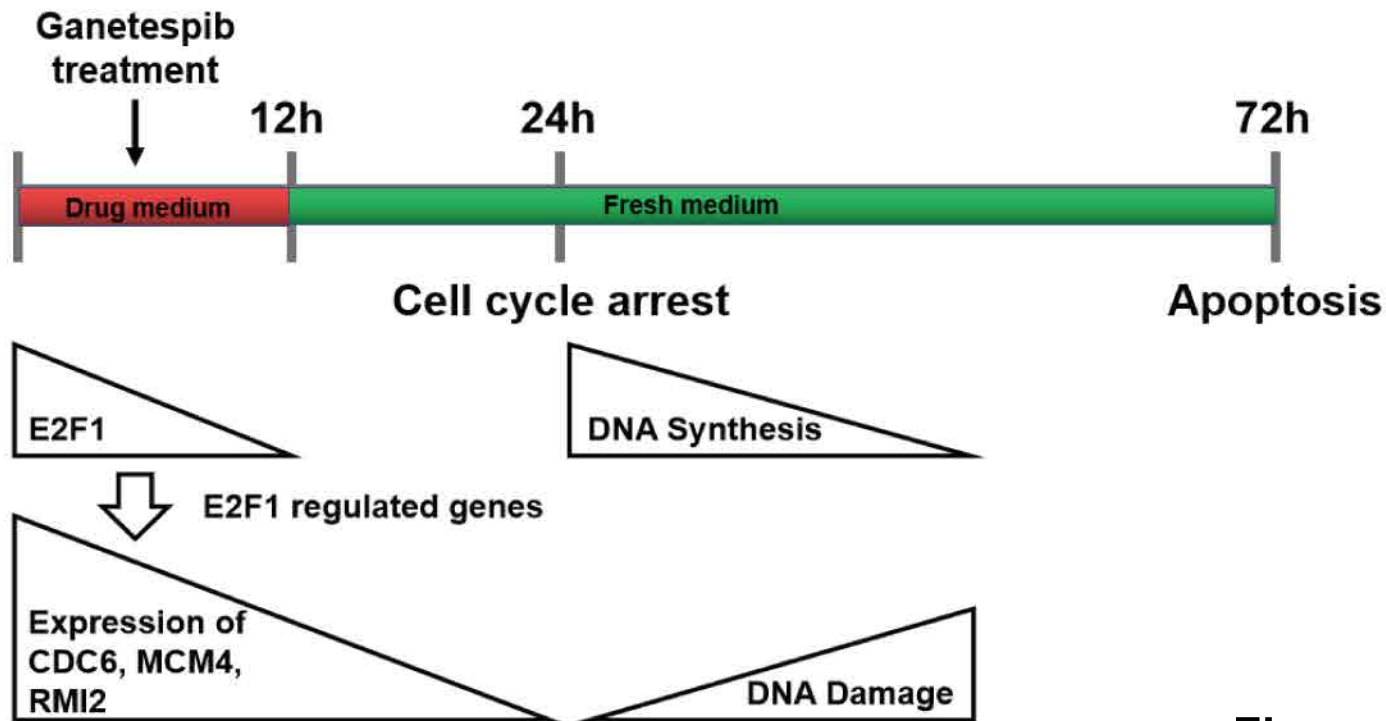


Figure S6