

Supplementary Table S1. List of DDX3 siRNA used in the study.

siRNA	Sequences, 5'→3'
#1	ccGuAuGcGuGAAuuAuAdTsdT uAuAAUUUcACGcAuACGGdTsdT
#2	uGcuGAAuGuAAAGAuGAdTsdT UcAAUCUuAcAUUcAGcAdTsdT
#3	AcAcuuGucuuGAGAuAuudTsdT AAuAUCUcAAGAcAAGUGUdTsdT
#4	AuGcGuGAAuuAuAuAuudTsdT AAuAuAuAAUUUcACGcAUdTsdT
#5	uGucuuGAGAuAuAAcGAdTsdT UCGUuAAuAUCUcAAGAcAdTsdT
#6	uGcAcAAGGuGucAAuucudTsdT AGAAUUGAcACCUUGUGcAdTsdT
#7	GuGuGAGcuuuuAAuGuuAdTsdT uAAcAUuAAAAGCUcAcACdTsdT
#8	AuuGGcGacuuGAAAcuAAdTsdT UuAGUUUcAAGUCGCcAAUdTsdT

control	cuuAcGcuGAGuAcuucGATsT UCGAAGuACUcAGCGuAAGTsT
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Upper case – ribonucleotide, lower case – 2'-O-methylribonucleotide, s –phosphorothioate group, T - thymidine.

Supplementary Table S2. List of primers used in the study.

Name	Forward, 5'→3'	Reverse, 5'→3'
GAPDH	TGCACCACCAACTGCTTAGC	GGCATGGACTGTGGTCATGAG
DDX3	CAACAGGCAACAACACTGTCCTCCAC	GAATAGCATGCTTCTGCACTGGAGTTG
DBP	GGA AAC AGC AAG CCC AAA GAA	CAG CGG CGC AAA AAG ACT C
CCNE1	GTG GCT CCG ACC TTT CAG TC	CAC AGT CTT GTC AAT CTT GGC A
CDKN1	CCT GGT GAT GTC CGA CCT G	CCA TGA GCG CAT CGC AAT C
MCM3	AGC GCA GAG AGA CTA CTT GGA	CAG CCG ATA CTG ATT GTC ACT
CTNNB1	ATGGAGCCGGACAGAAAAGC	TGGGAGGTGTCAACATCTTCTT
GSK3	GCGTTCCCAAGAAGTGGCTTA	GGTCCAGCTTACGCATAATCTG
ELOVL3	TTC TCA CGC GGG TTA AAA ATG G	GAG CAA CAG ATA GAC GAC CAC
MMP10	GAG CCA CTA GCC ATC CTG G	CTG AGC AAG ATC CAT GCT TGG
C-MYC	GTC AAG AGG CGA ACA CAC AAC	TTG GAC GGA CAG GAT GTA TGC
TNF-A	AGC CCC CAG TCT GTA TCC TT	GGT CAC TGT CCC AGC ATC TT
PYGO-1	CCA TCG CGC TGA AGA GAG TTA	GTG TGT TGG CCT TGC GTT TT
PDK4	AGG GAG GTC GAG CTG TTC TC	GGA GTG TTC ACT AAG CGG TCA

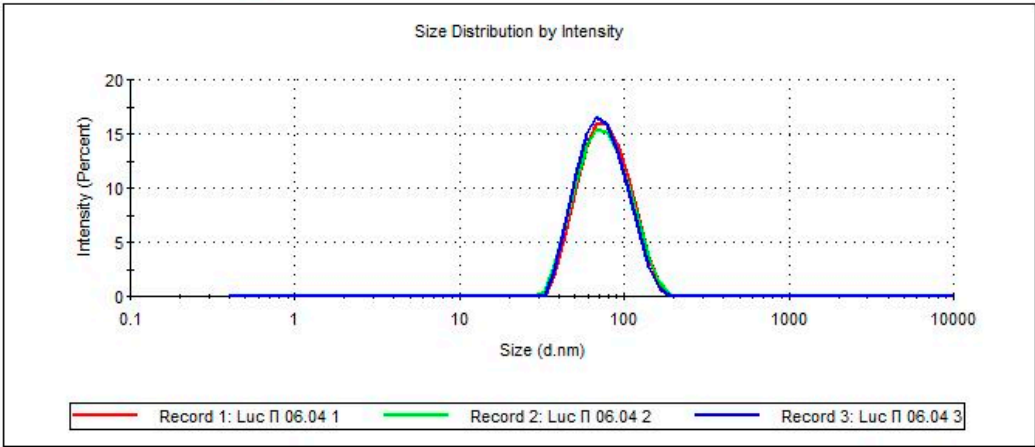
Upper case – 2'-deoxynucleotide.

Supplementary Table S3. Characterization of LNP-siRNA used in the study.

	LNP size	siRNA concentration, ng/μl	siRNA entrapment efficiency
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LNP-control

	Size (d.nm):	% Intensity:	St Dev (d.nm):
Z-Average (d.nm): 72,17	Peak 1: 79,77	100,0	26,86
Pdl: 0,125	Peak 2: 0,000	0,0	0,000
Intercept: 0,929	Peak 3: 0,000	0,0	0,000
Result quality : Good			

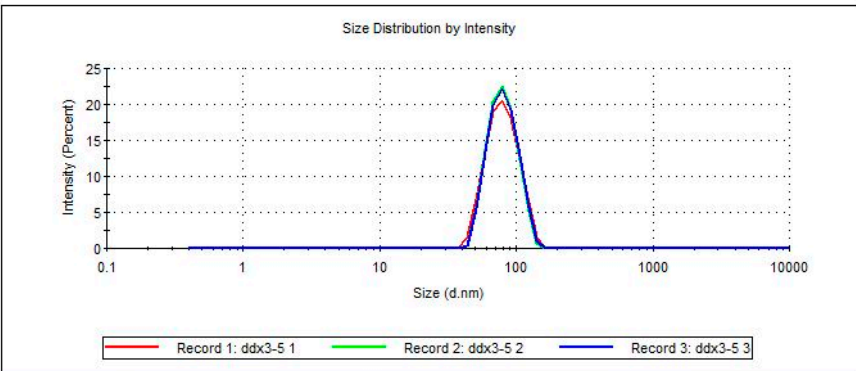


137

63%

LNP-siRNA#5

	Size (d.nm):	% Intensity:	St Dev (d.nm):
Z-Average (d.nm): 75,93	Peak 1: 80,87	100,0	21,15
Pdl: 0,049	Peak 2: 0,000	0,0	0,000
Intercept: 0,936	Peak 3: 0,000	0,0	0,000
Result quality : Good			

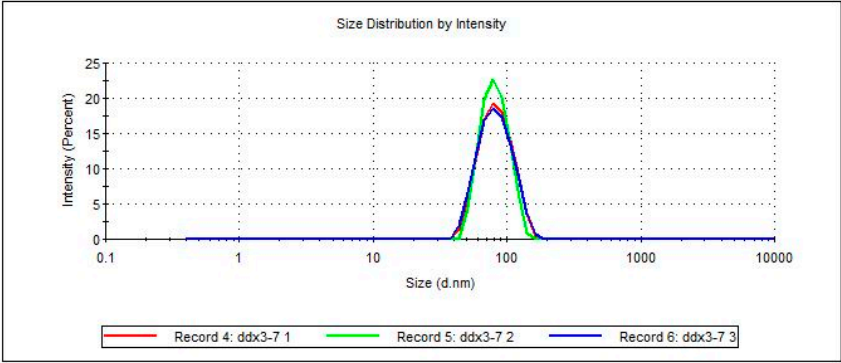


123.5

57%

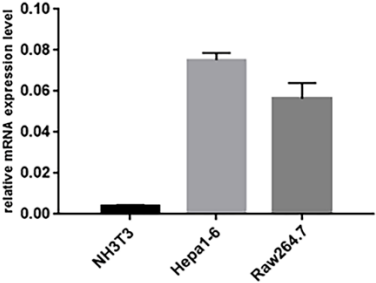
LNP-siRNA#7

	Size (d.nm):	% Intensity:	St Dev (d.nm):
Z-Average (d.nm): 78,62	Peak 1: 84,85	100,0	23,79
Pdi: 0,072	Peak 2: 0,000	0,0	0,000
Intercept: 0,963	Peak 3: 0,000	0,0	0,000
Result quality : Good			

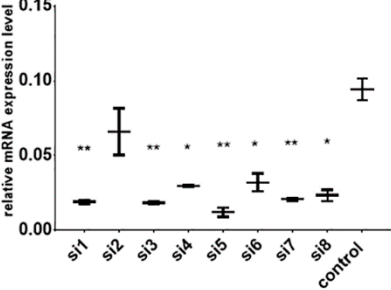


134.5

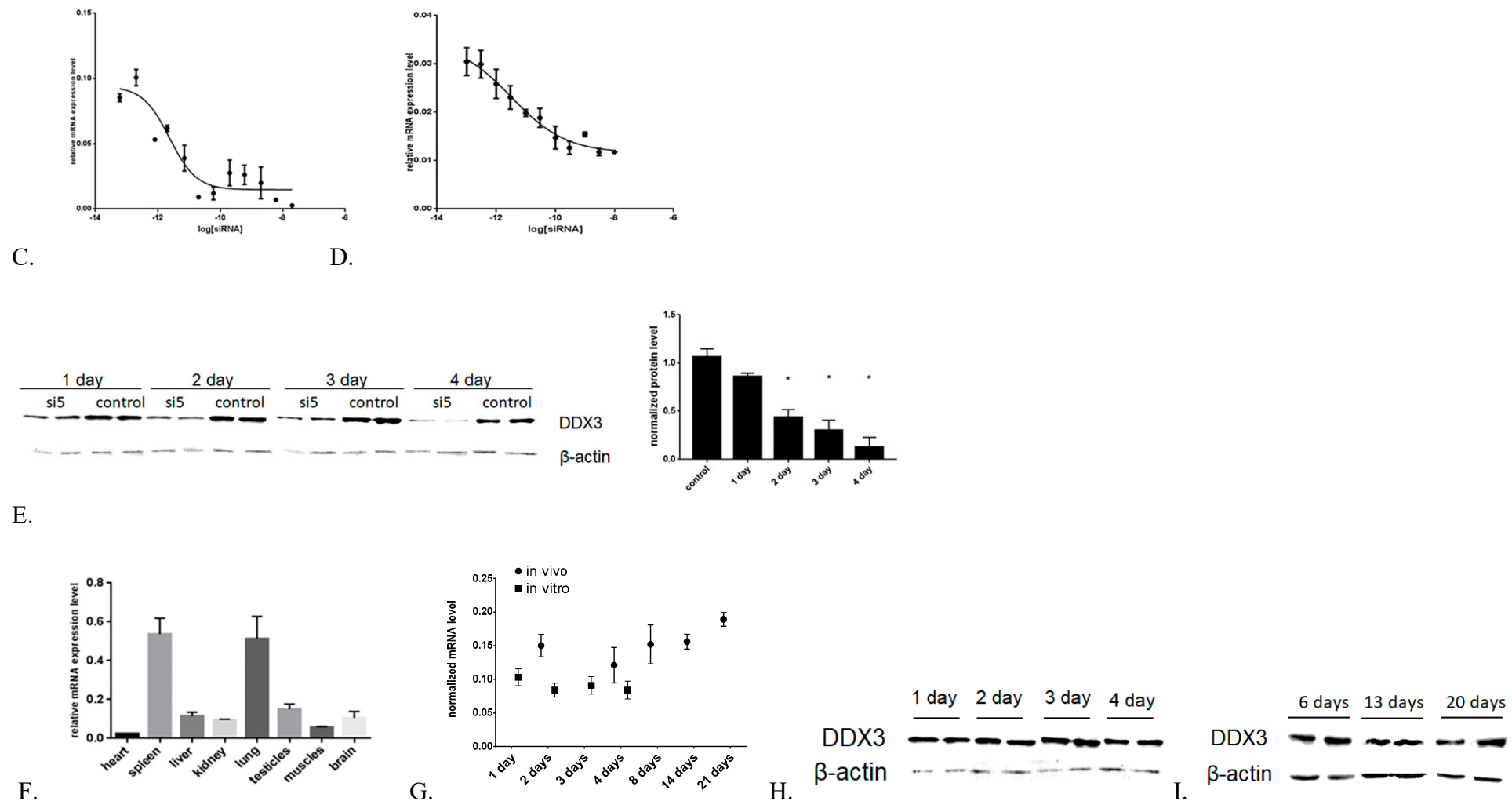
62%



A.

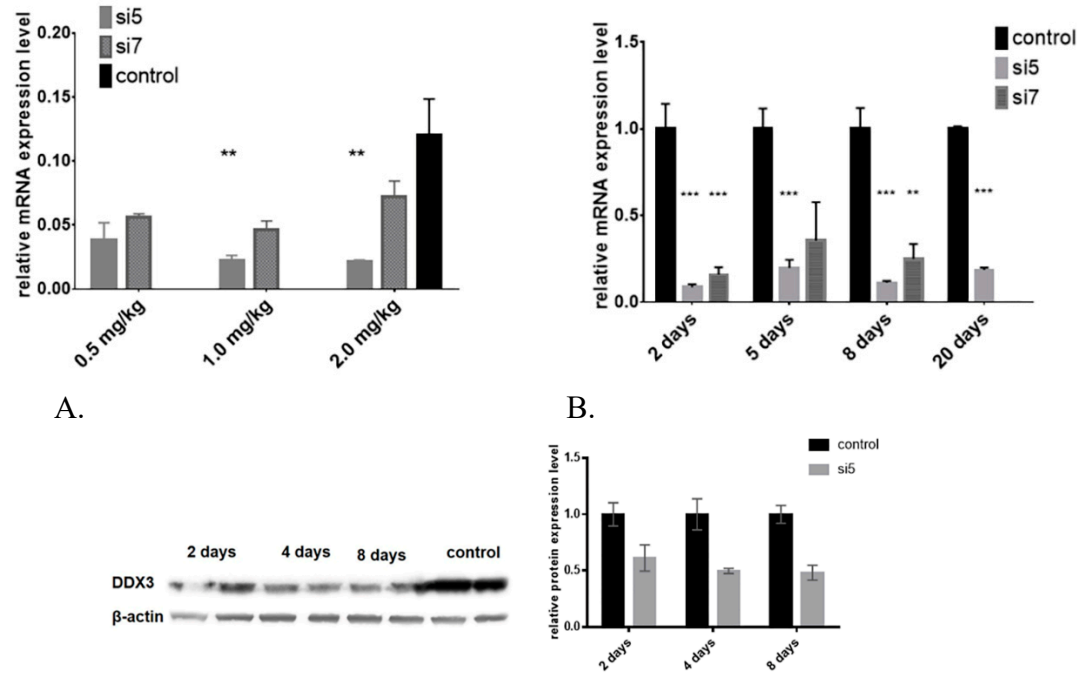


B.



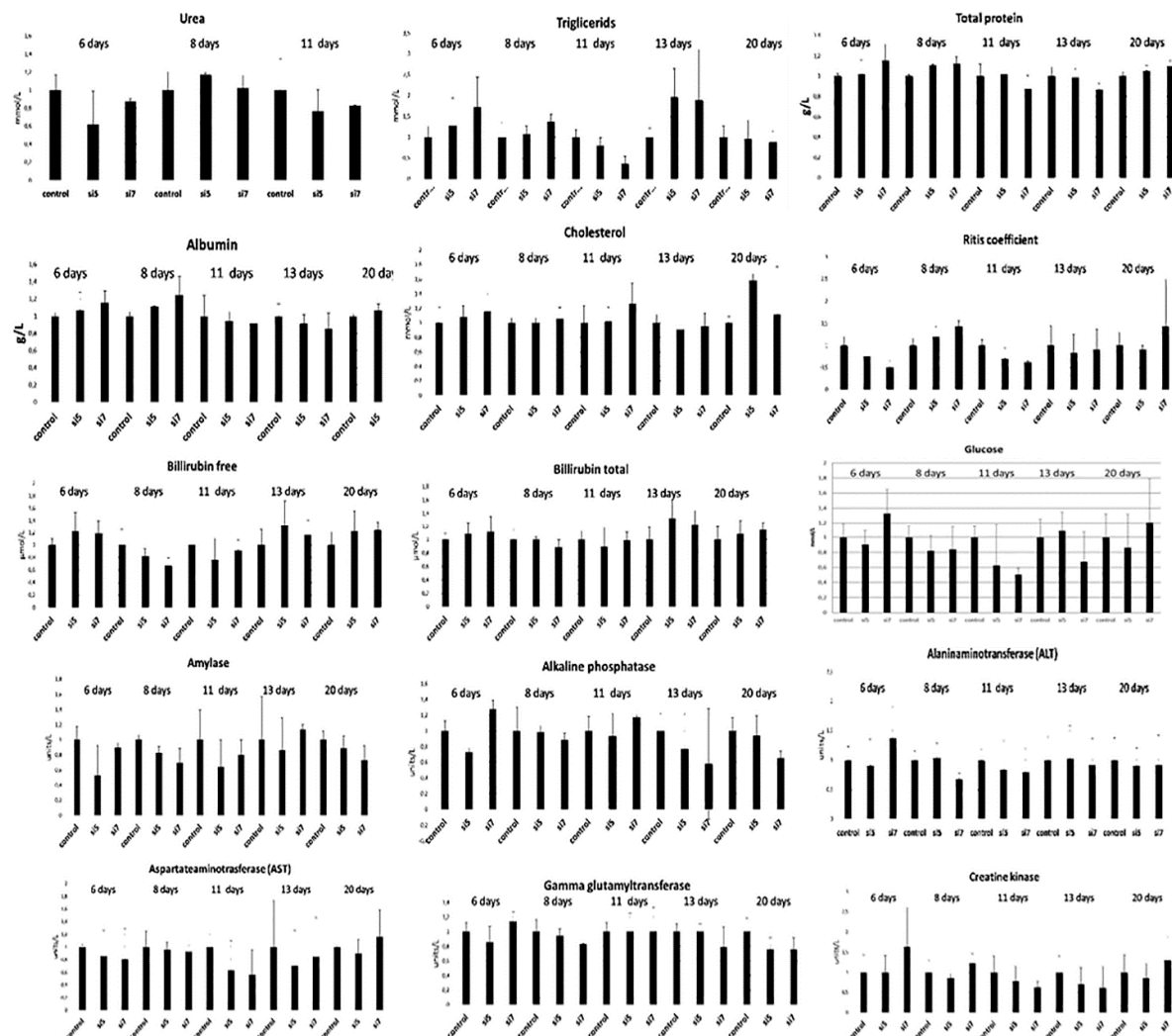
Supplementary Figure S1. A. Determination of the DDX3 mRNA expression level in different cell lines by RT-qPCR. B. Determination of the DDX3 siRNA efficacy in Hepa1-6 cells by RT-qPCR (* $p < 0.05$, ** $p < 0.01$). 1-8 are the numbers of siRNA from Suppl. table 1. Estimation IC₅₀ for si#5 (C.) and si#7 (D.) in Hepa1-6 cells by RT-qPCR. E. Determination the efficacy of the DDX3 protein inhibition in Hepa1-6 cells by Western-blot. F. Estimation DDX3 mRNA expression level in different murine organs by RT-qPCR. G. Estimation DDX3 mRNA expression level at the different time points after

the siLuc treatment (control siRNA) *in vitro* and *in vivo* by RT-qPCR. Determination the DDX3 protein level at the different time points after siLuc (control siRNA) treatment *in vitro* (H.) and *in vivo* (I.) by Western-blot.



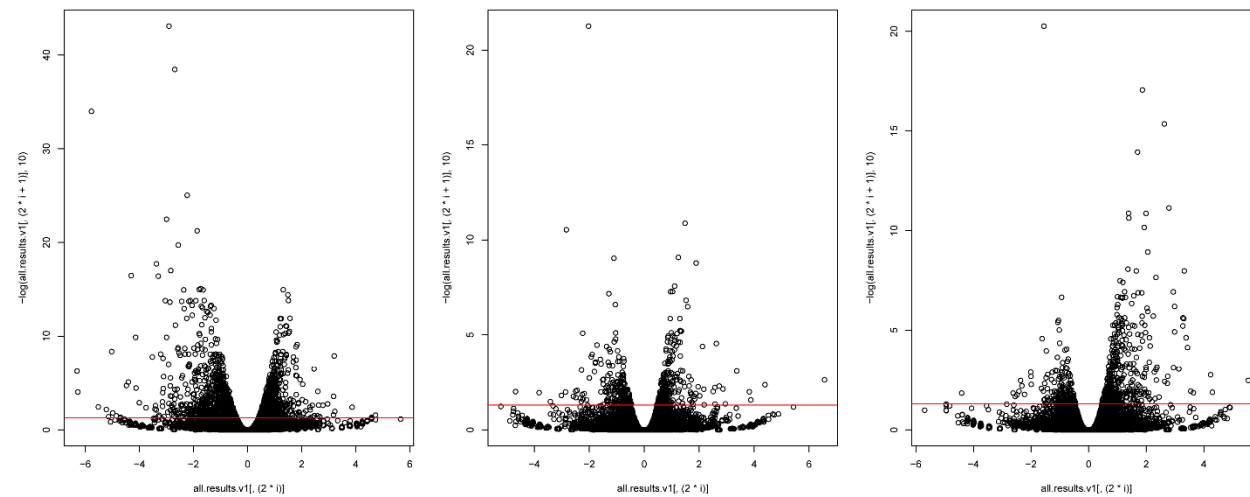
C.

Supplementary Figure S2. A. Estimation of the dose response for si#5 and si#7 by RT-qPCR in the murine liver. B. Determination of DDX3 mRNA recovery after RNAi-mediated inhibition by si#5 and si#7 by RT-qPCR. C. Determination the efficacy of DDX3 protein inhibition by Western-blot. *p<0.05, **p<0.01, ***p<0.001.

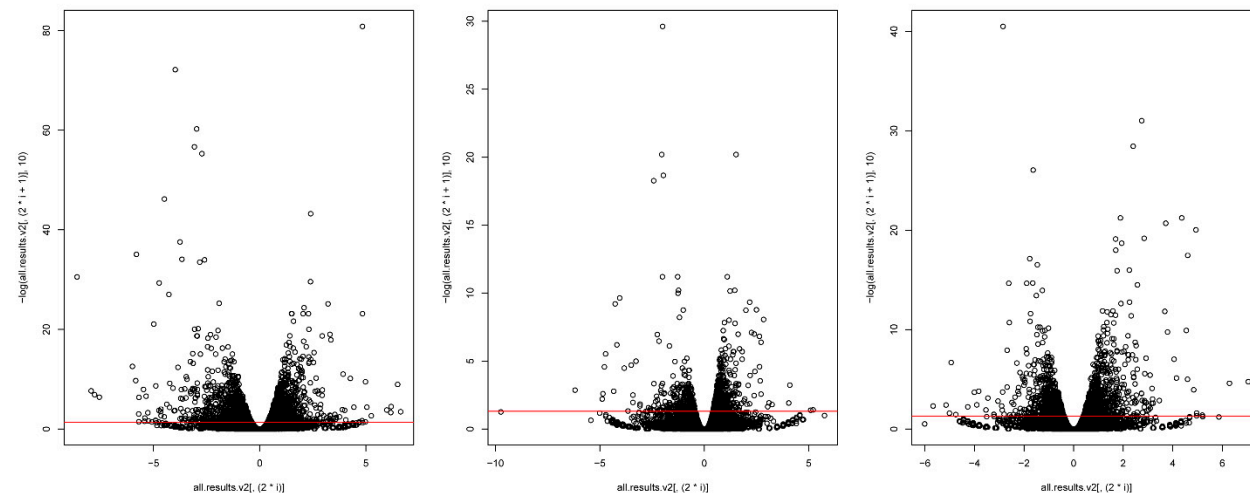


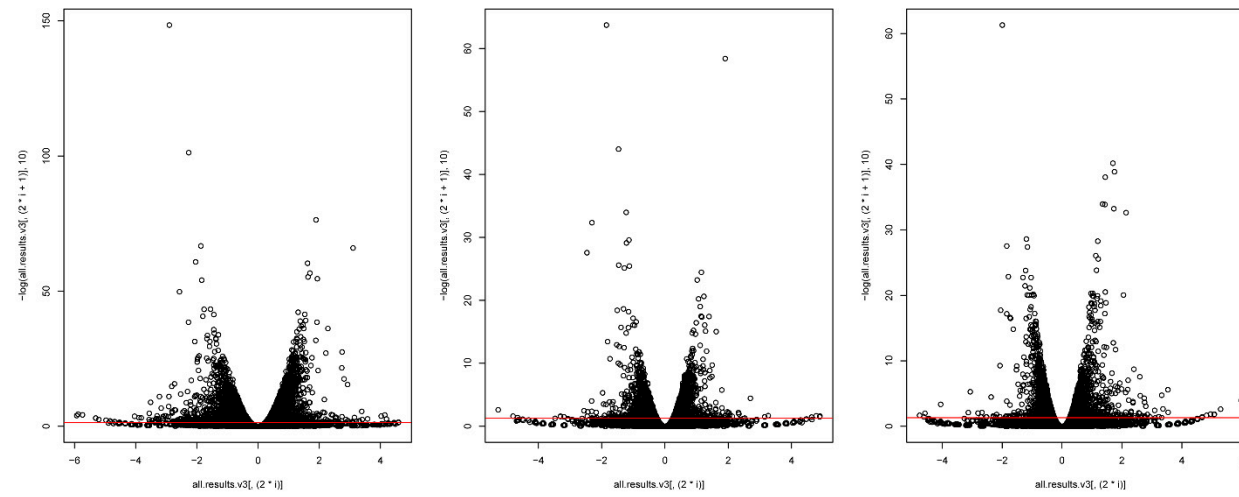
Supplementary Figure S3. Liver biochemical markers analyzed in animal blood after the administration of si#5 and si#7 biweekly for 3 weeks.

A.



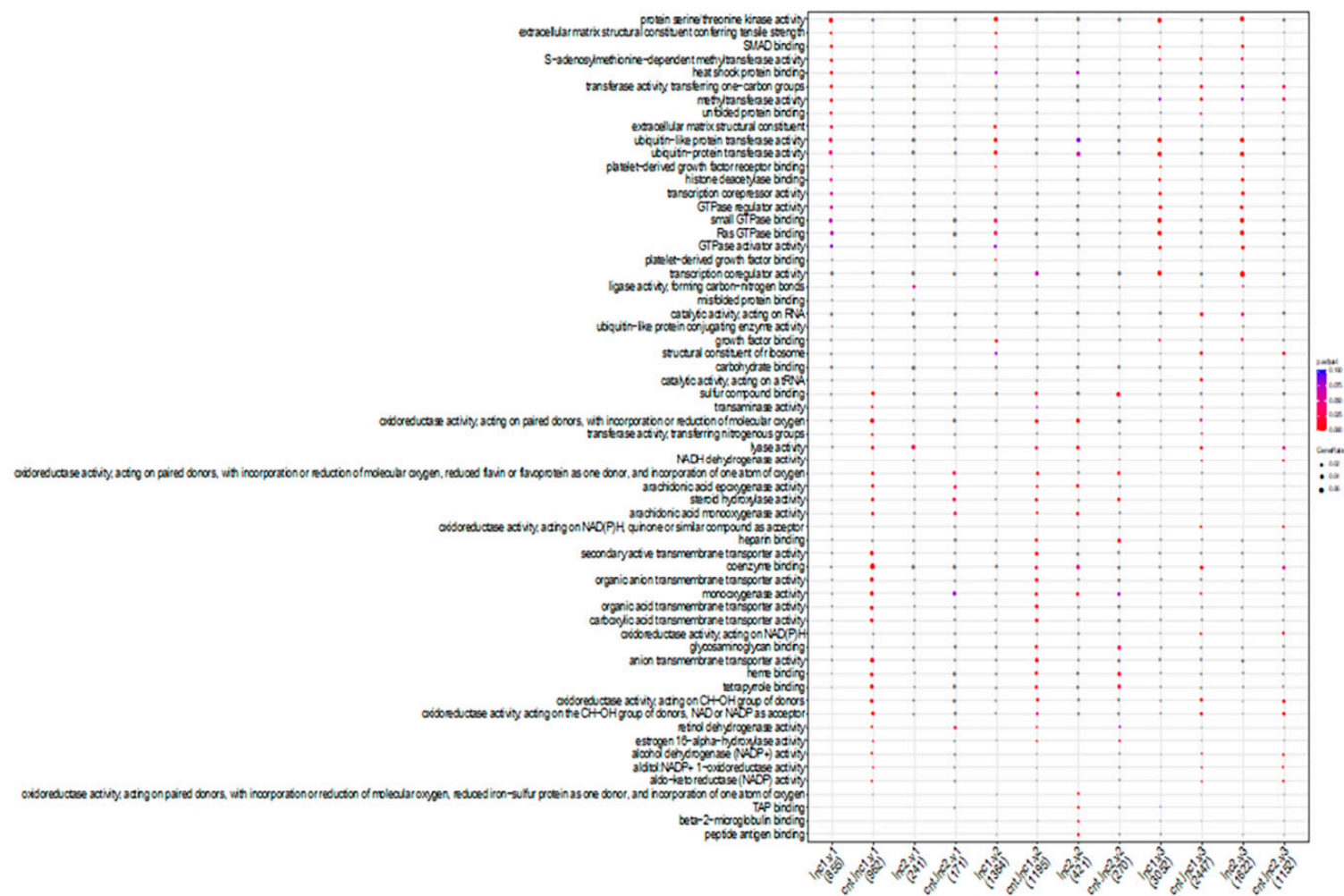
B.





C.

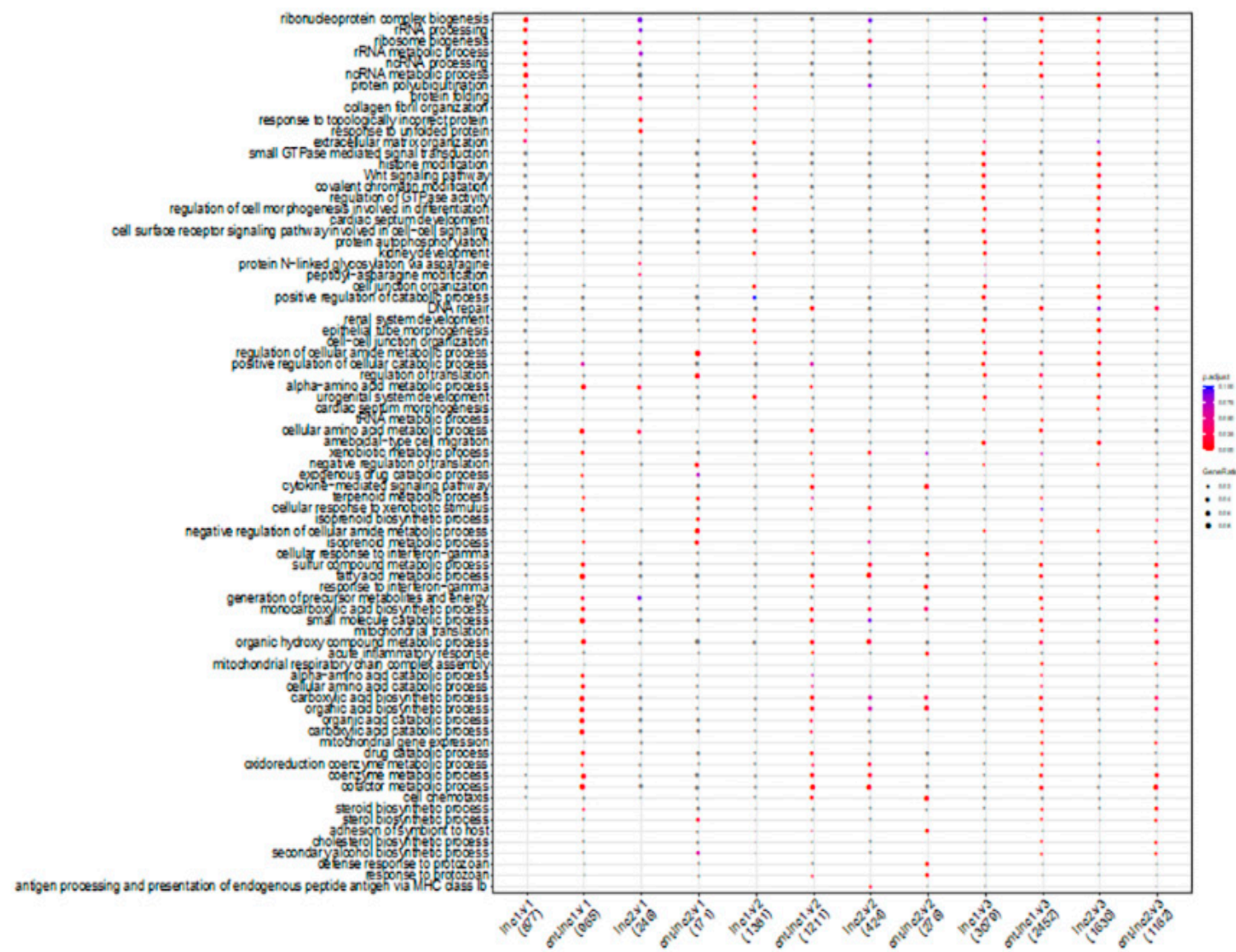
Supplementary Figure S4. Volcano plots of gene expression after DDX3 depletion by siRNA #5 and siRNA #7 in A. cells, B. liver day 6, C. liver day 13.



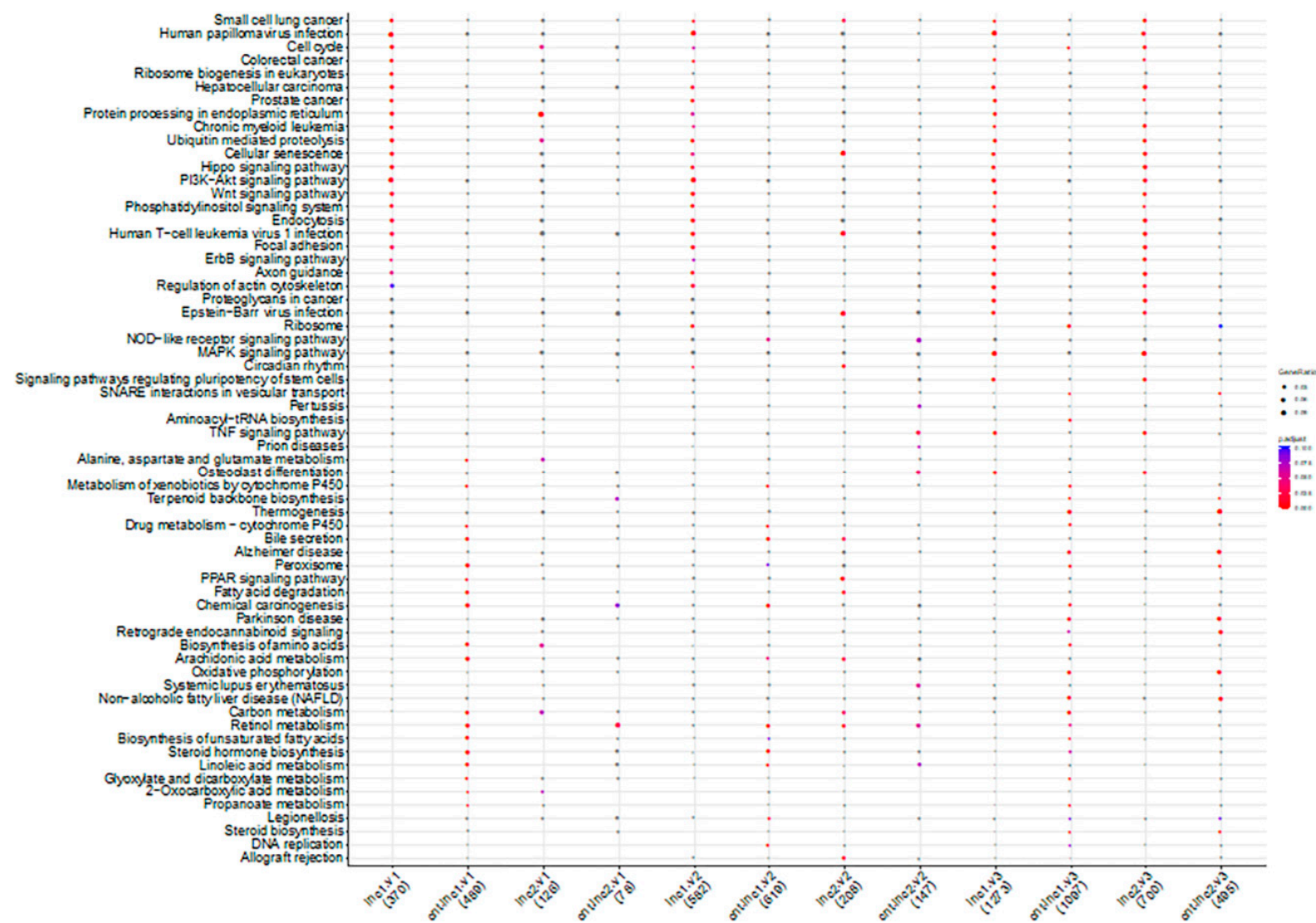
A.



B.



C.



D.

Supplementary Figure S5. Gene ontology analysis of gene expression after DDX3 depletion (KD) by siRNA #5 and siRNA #7: A. molecular functions (MF), B. Cellular components (CC), C. Biological pathways (BP), D. KEGG. v1 marked liver samples at 6th day of DDX3 KD, v2 – liver samples at 13th day of DDX3 KD, v3 – cells after DDX3 KD. Lnc1 is siRNA #5, lnc2 – siRNA #7, cntrl – control cells.