Ingredient	AIN-93M diet	60% high-fat diet
Casein, g	14.00	14.00
L-Cystine, g	0.18	0.18
Corn starch, g	46.57	13.57
Maltodextrin, g	15.50	15.50
Sucrose, g	10.00	10.00
Cellulose, g	5.00	5.00
Soybean oil, g	4.00	37.00
Mineral mix, g	3.50	3.50
Vitamin mix, g	1.00	1.00
Choline bitartrate, g	0.25	0.25
Antioxidants, g	10.00	10.00
Total, g	100.00	100.00
Fat energy, %	10.00	60.00
Energy, kcal/g	3.60	5.50

Table S1. Compositions of AIN-93M diet and 60% high-fat diet.





Figure S2. GSVA analysis of kidney tissue.



Figure S3. GSVA analysis of colon tissue.















Figure S7. The top 5 significant GO terms enriched in rescue DEGs in each tissue by low dose MK-7 intervention (left) and Venn diagrams show the overlapping rescue

DEGs among six groups (right).



Figure S8. Top 5 significant GO terms enriched in rescue DEGs in each tissue by high dose MK-7 intervention (left) and Venn diagrams show the overlapping rescue





Figure S9. Venn diagram shows the overlapping rescue DEGs between LVK Rescue DEGs and HVK Rescue DEGs.

Figure S10. Changes in core regulatory transcription factors during obesity and high dose MK-7 intervention. (A) Heatmap shows the activity of the regulatory transcription factor networks (regulon). Core (top 5 significant differential networks or top 5 size of the differential networks) regulons are highlighted with two different colors. Red represents the upregulated activity of the regulon compared to HF group and blue represents the downregulated activity of the regulon compared to HF group. (B) Bar plot shows the amount of significant differential regulons in HVK group compared with the HF group. Venn diagram (left) shows the overlapping upregulated regulons among 6 tissues and Venn diagram (right) shows the overlapping downregulated regulons among 6 tissues. Dot plot (top) shows the GO terms enriched in upregulated regulons in each tissue and dot plot (bottom) shows the GO terms enriched in downregulated regulons in each tissue.



Figure S11. Erased tissue-tissue ligand	-receptor pairs upon 1	low-dose MK-7 intervention (LVK).	
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SourceTarget	Interaction	Source Target	Interaction	Source Target Interaction	Source Target Interaction	Source Target	Interaction
Brain Heart	Alcam - Cd6	Kidney Brain	Dsg2 - Dsc3	Colon Kidney Gm7030 - Cd8b1	Heart Kidney H2-t24 - Cd8b1	Colon Brain	Nectin2 - Cd226
Heart Liver	Cd200 - Cd200r1	Liver Kidney	Efna1 - Epha1	Kidney Kidney Gm7030 - Cd8b1	Colon Muscle H2-t3 - Cd8a	Kidney Colon	Nectin2 - Cd226
Muscle Colon	Cd200 - Cd200r4	Liver Liver	Efna1 - Epha1	Heart Colon H2-aa - Cd4	Colon Kidney H2-t-ps - Cd8b1	Liver Heart	Nectin2 - Cd226
Kidney Liver	Cd209a - Ceacam1	Kidney Heart	Efna1 - Epha4	Colon Heart H2-aa - Cd4	Kidney Kidney Icam1 - (Itgal+Itgb2)	Colon Heart	Nectin2 - Tigit
Colon Brain	Cd22 - Ptprc	Brain Brain	Efna1 - Epha5	Colon Liver H2-aa - Cd4	Heart Heart Icam1 - (Itgam+Itgb2)	Heart Brain	Nfasc - (Cntn1+Cntnap1)
Colon Muscle	Cd22 - Ptprc	Colon Heart	Efna1 - Epha7	Colon Heart H2-ab1 - Cd4	Kidney Heart Icam1 - (Itgam+Itgb2)	Brain Liver	Nrxn1 - Nlgn2
Heart Brain	Cd274 - Pdcd1	Brain Brain	Efna1 - Epha8	Colon Liver H2-ab1 - Cd4	Kidney Kidney Icam1 - (Itgam+Itgb2I)	Brain Heart	Nrxn1 - Nlgn3
Colon Heart	Cd48 - Cd244a	Brain Heart	Efna2 - Epha3	Brain Kidney H2-bl - Cd8a	Kidney Heart Icam1 - (Itgax+Itgb2)	Brain Liver	Nrxn3 - Nlan2
Colon Muscle	Cd52 - Siglecg	Brain Colon	Efna2 - Epha4	Brain Kidney H2-bl - Cd8b1	Heart Kidney Icam1 - (Itgax+Itgb2)	Colon Liver	Pdcd1la2 - Pdcd1
Heart Brain	Cd6 - Alcam	Brain Colon	Efna2 - Epha7	Colon Kidney H2-bl - Cd8b1	Kidney Liver Icam1 - (Itgax+Itgb2)	Brain Colon	Ptorc - Cd22
Colon Liver	Cdh1 - (Itga1+Itgb1)	Brain Liver	Efna2 - Epha7	Brain Colon H2-d1 - Cd8a	Kidney Heart Icam1 - Spn	Muscle Colon	Ptprc - Cd22
Colon Heart	Cdh1 - (Itgae+Itgb7)	Liver Brain	Efna2 - Epha8	Brain Colon H2-d1 - Cd8b1	Kidney Liver Icam2 - (Itgal+Itgb2)	Kidney Heart	Ptorc - Mrc1
Colon Heart	Cdh1 - Kira1	Brain Muscle	Efna3 - Enha2	Colon Kidney H2-d1 - Cd8b1	Muscle Liver Icam2 - (Itgal+Itgb2)	Brain Brain	Ptorm - Ptorm
Colon Kidney	Clec2d - Kirb1b	Kidney Brain	Efna3 - Epha3	Colon Heart H2-dma - Cd4	Kidney Liver Icam2 - (Itgal+Itgb2I)	Kidney Colon	Sele - Cd44
Liver Kidney	Clec2d - Kirb1b	Brain Heart	Efna3 - Enha3	Colon Liver H2-dma - Cd4	Muscle Liver Icam2 - (Itgal+Itgb2I)	Kidney Colon	Sele - Ceacam1
Kidney Kidney	Clec2i - Kirb1f	Brain Kidney	Efna3 - Enha3	Kidney Heart H2-dmh1 - Cd4	Heart Kidney Icam2 - (Itgam+Itgb2)	Liver Heart	Selpla - Sele
Brain Heart	Coto1 - Nrcam	Brain Muscle	Efna3 - Enha3	Colon Liver H2-dmb1 - Cd4	Brain Muscle Icosl - Cd28	Muscle Heart	Selpig - Sele
Heart Brain	Coto2 - L1cam	Kidney Brain	Efna3 - Enha4	Kidney Liver H2-dmb1 - Cd4	Liver Liver Itab2 - Cd226	Brain Kidney	Selpig - Sele
Brain Heart	Coto2 - L1cam	Kidney Brain	Efna3 - Enha5	Colon Kidney H2-dmb2 - Cd4	Kidney Kidney Itab2 - Icam1	Brain Heart	Selpig - Selp
Kidney Kidney	Csno4 - (Itaa2+Itab1)	Kidney Brain	Efna3 - Enha7	Colon Liver H2-dmb2 - Cd4	Liver Kidney Itab2 Icam2	Colon Heart	Selpig Selp
Brain Brain	DII1 - Notch1	Brain Kidney	Efna3 - Enha7	Colon Heart H2-eb1 - Cd4	Liver Muscle Itch2 - Icam2	Kidney Kidney	Sema4a - (Nrn1+Plyna1)
Kidney Brain	DII1 - Notch1	Brain Muscle	Efna3 - Epha7	Colon Liver H2-ob1 - Cd4	Liver Liver Itab21 - Cd226	Kidney Kidney	Sema4a - Plynb1
Brain Heart	DII1 - Notch1	Brain Brain	Efna4 - Enha4	Colon Kidney H2-k1 - Cd8b1	Liver Kidney Itab2I - Icam2	Kidney Liver	Sema4a - Plynh1
Colon Heart	DII1 - Notch1	Kidney Heart	Efna4 - Epha4	Liver Kidney H2-k1 - Cd8b1	Liver Muscle Itab21 - Icam2	Brain Kidney	Sema4d - Cd72
Heart Heart	DII1 - Notch1	Liver Liver	Efna5 - Enhal	Kidney Muscle H2-m1 - Cd8a	Brain Heart Jan1 - Notch1	Brain Kidney	Sema4d - Plynh1
Kidney Heart	DII1 - Notch1	Kidney Colon	Efna5 - Enha?	Colon Heart H2-m2 - Cd8a	Heart Brain Jag1 - Notch?	Brain Liver	Sema4d - Plynh1
Muscle Heart	DII1 - Notch1	Liver Heart	Efna5 - Enha4	Colon Colon H2-m5 - Cd8a	Kidney Brain lag1 - Notch2	Liver Liver	Sema4a - Plynh2
Kidney Brain	DII1 - Notch2	Kidney Brain	Efna5 - Enhb2	Kidney Colon H2-m5 - Cd8a	Kidney Heart Jag1 - Notch2	Brain Muscle	Sema5a - Pixna1
Kidney Heart	DII1 - Notch2	Kidney Colon	Efna5 - Ephb2	Brain Heart H2-m5 - Cd8a	Kidney Muscle Jag1 - Notch4	Muscle Brain	Sema5a - Plynh3
Brain Kidney	DII1 - Notch2	Liver Brain	Efnh1 - Enhh3	Colon Colon H2-m5 - Cd8h1	Brain Brain Jag2 - Notch1	Brain Colon	Sema6a - Plyna2
Colon Kidney	DII1 - Notch2	Kidney Brain	Efnb2 - Enha4	Brain Heart H2-m5 - Cd8h1	Brain Heart Jan2 - Notch2	Brain Heart	Sema6a - Pixna2
Kidney Kidney	DII1 - Notch2	Heart Brain	Efnb2 - Enhb2	Muscle Muscle H2-m9 - Cd8a	Liver Liver Jam1 - (Itgal+Itgb2)	Brain Heart	Sema6a - Pixna4
Brain Liver	DII1 - Notch2	Heart Colon	Efnb2 - Ephb3	Colon Kidney H2-oa - Cd4	Brain Kidney Jam2 - (Itga3+Itgh1)	Muscle Brain	Sema6h - Plyna4
Kidney Liver	DII1 - Notch2	Brain Heart	Efnb2 - Enhb3	Colon Liver H2-oa - Cd4	Brain Kidney Jam2 - E11r	Brain Colon S	Sema6d - (Plxna1+Trem2)
Brain Heart	DII1 - Notch3	Brain Kidney	Efnb2 - Ephb3	Kidney Colon H2-ob - Cd4	Kidney Heart Jam3 - (Itgam+Itgb2)	Brain Muscle	Sema6d - Pixna1
Colon Heart	DII1 - Notch3	Colon Muscle	Efnb2 - Enhb4	Colon Kidney H2-ob - Cd4	Kidney Liver Jam3 - E11r	Colon Kidney	Sema7a - (Itob1+Itga1)
Heart Heart	DII1 - Notch3	Colon Heart	Entod1 - Adora2a	Colon Liver H2-ob - Cd4	Colon Brain 1cam - (Itoa4+Itob7)	Brain Heart	Sema7a - Plxnc1
Kidney Heart	DII1 - Notch3	Kidney Heart	Entod1 - Adora2a	Muscle Colon H2-01 - Cd8a	Brain Heart L1cam - (Itoav+Itob3)	Colon Liver	Sema7a - Plxnc1
Muscle Heart	DII1 - Notch3	Kidney Brain	Entod1 - Adora2h	Heart Colon H2-g1 - Cd8b1	Colon Heart L1cam - (Itgav+Itgb3)	Liver Heart	Sidlec1 - Snn
Kidney Muscle	DII1 - Notch3	Brain Kidney	Entod1 - Adora2b	Colon Heart H2-g1 - Cd8b1	Brain Muscle I 1cam - (Itgav+Itgb3)	Heart Colon	Tigit - Nectin2
Brain Heart	DII1 - Notch4	Brain Brain	Entod1 - Tmiad3	Liver Kidney H2-g1 - Cd8b1	Kidney Brain L1cam L1cam	Brain Colon	Ulbp1 - (Kirk1+Hcst)
Colon Heart	DII1 - Notch4	Colon Brain	Entpd1 - Tmigd3	Colon Colon H2-rd10 - Cd8a	Brain Kidney L1cam - L1cam	Brain Brain	Vcam1 - (Itga4+Itgb1)
Heart Heart	DII1 - Notch4	Kidney Brain	Entod1 - Tmigd3	Liver Heart H2-g10 - Cd8b1	Heart Colon Lck - (Cd8a+Cd8h1)	Heart Heart	Vcam1 - (ltga4+ltgb1)
Kidney Heart	DII1 - Notch4	Liver Brain	Entod1 - Tmigd3	Colon Muscle H2-n2 - Cd8a	Colon Heart Lok - (Cd8a+Cd8b1)	Liver Heart	Vcam1 - (Itga4+Itgb1)
Muscle Heart	DII1 - Notch4	Muscle Brain	Entod1 - Tmigd3	Heart Kidney H2-rd - Cd8b1	Brain Liver Lrrc4 - Ntng2	Brain Brain	Vcam1 - (Itga1+Itgb7)
Kidney Kidney	DII1 - Notch4	Kidney Brain	E11r - Jam2	Liver Kidney H2-g7 - Cd8b1	Muscle Kidney Moz - Moz	Brain Heart	Vcam1 - (Itga4+Itgb7)
Heart Liver	DII4 - Notch1	Liver Kidney	E11r - Jam3	Muscle Colon H2-t10 - Cd8b1	Kidney Muscle Moz - Moz	Liver Heart	Vcam1 - (Itga4+Itgb7)
Colon Heart	DII4 - Notch2	Liver Colon	Gm10499 - Cd8a	Liver Kidney H2-110 - Cd8h1	Brain Brain Mozl1 - Mozl1	Liver Brain	Vcam1 - (Itaa9+Itab1)
Muscle Brain	Dag1c - Dac3	Liver Colon	Gm10499 - Cd8h1	Colon Kidney H2-123 - Cd8b1	Brain Heart Ncam1 - L1cam	Kidney Heart	Vcam1 - (Itga9+Itgb1)
Liver Heart	Dsg1c - Dsc3	Kidney Heart	Gm11127 - Cd8a	Liver Kidney H2-t23 - Cd8h1	Brain Heart Ncam2 - L1cam	Muscle Heart	Vcam1 - (Itga9+Itgb1)
Liver right	55910 5550	. anoy near	San The Good		arean from from the croom	Heart Kidney	Vcam1 - (Itga9+Itgb1)
		2.7				Colon Kidney	Vsir - Igsf11

Figure S12. Erased tissue-tissue ligand-receptor pairs upon high-dose MK-7 intervention (LVK).

Source	Target	Interaction	Source	Target	Interaction	Source	Target	Interaction
Brain	Heart	Alcam - Cd6	Kidney	Kidney	ltgb2 - lcam1	Kidney	Heart	DII1 - Notch2
Heart	Liver	Cd200 - Cd200r1	Liver	Muscle	ltgb2 - Icam2	Brain	Liver	Nrxn1 - Nlgn2
Muscle	Colon	Cd200 - Cd200r4	Liver	Liver	Itgb2l - Cd226	Brain	Liver	Nrxn3 - Nlgn2
Kidney	Heart	Entpd1 - Adora2a	Liver	Muscle	Itgb2I - Icam2	Heart	Brain	Cd274 - Pdcd1
Kidney	Brain	Entpd1 - Adora2b	Liver	Liver	Jam1 - (Itgal+Itgb2)	Liver	Heart	Selpig - Sele
Kidney	Brain	Entpd1 - Tmigd3	Kidney	Brain	F11r - Jam2	Muscle	Heart	Selpig - Sele
Liver	Brain	Entpd1 - Tmigd3	Brain	Kidney	Jam2 - F11r	Colon	Heart	Selpig - Selp
Kidney	Heart	Ptprc - Mrc1	Brain	Muscle	L1cam - (Itgav+Itgb3)	Kidney	Kidney	Sema4a - (Nrp1+Plxna1)
Colon	Muscle	Cd52 - Siglecg	Kidney	Brain	L1cam - L1cam	Kidney	Liver	Sema4a - Plxnb1
Heart	Brain	Cd6 - Alcam	Brain	Kidney	L1cam - L1cam	Brain	Kidney	Sema4d - Cd72
Colon	Liver	Cdh1 - (ltga1+ltgb1)	Heart	Colon	Lck - (Cd8a+Cd8b1)	Muscle	Brain	Sema5a - Plxnb3
Colon	Heart	Cdh1 - Kirg1	Muscle	Muscle	H2-m9 - Cd8a	Colon	Kidney	Sema7a - (Itgb1+Itga1)
Kidnev	Liver	Cd209a - Ceacam1	Muscle	Colon	H2-g1 - Cd8a	Colon	Liver	Sema7a - Plxnc1
Colon	Kidnev	Clec2d - Kirb1b	Colon	Colon	H2-q10 - Cd8a	Liver	Heart	Siglec1 - Spn
Liver	Kidney	Clec2d - Kirb1b	Colon	Muscle	H2-g2 - Cd8a	Heart	Colon	Tigit - Nectin2
Kidnev	Kidney	Clec2i - Kirb1f	Colon	Muscle	H2-t3 - Cd8a	Brain	Brain	Vcam1 - (ltga4+ltgb1)
Heart	Brain	Nfasc - (Cntn1+Cntnap1)	Kidney	Muscle	H2-m1 - Cd8a	Liver	Brain	Vcam1 - (ltga9+ltgb1)
Brain	Heart	Cntn1 - Nrcam	Brain	Kidney	H2-bl - Cd8a	Brain	Brain	Vcam1 - (ltga4+ltgb7)
Kidney	Kidney	Cspg4 - (Itga2+Itgb1)	Liver	Colon	Gm10499 - Cd8a	Brain	Heart	Vcam1 - (ltga4+ltgb7)
Muscle	Brain	Dsg1c - Dsc3	Brain	Heart	H2-m5 - Cd8a	Heart	Colon	Adare5 - Cd55b
Kidney	Brain	Dsg2 - Dsc3	Liver	Kidney	H2-t23 - Cd8b1	Kidney	Colon	Adare5 - Cd55b
Kidney	Heart	Efna1 - Enha4	Heart	Kidney	H2-t24 - Cd8b1	Liver	Colon	Adgre5 - Cd55b
Brain	Brain	Efna1 - Enha5	Liver	Kidney	H2-t10 - Cd8b1	Muscle	Colon	Adgre5 - Cd55b
Colon	Heart	Efnal - Enha7	Brain	Kidney	H2-bL - Cd8b1	Brain	Kidney	Alcam - Cd6
Brain	Brain	Efnal - Enha8	Brain	Colon	H2-d1 - Cd8b1	Musclo	Brain	Entrol1 - Adora2b
Brain	Liver	Efna? - Enha7	Colon	Kidney	H2-d1 - Cd8b1	Kidney	Brain	Cd6 - Alcam
Liver	Brain	Efna2 - Epha8	Colon	Kidney	H2-k1 - Cd8b1	Color	Brain	Cdb1 - (Itgae+Itgb7)
Brain	Muselo	Efna3 - Enha2	Liver	Kidnov	H2-k1 - Cd8b1		Drain	Guilt (ligac ligs))
Brain	Muscle	Efna3 - Epha3	Liver	Colon	Gm10499 - Cd8b1			
Kidnov	Broin	Efna3 Ephad	Hoart	Kidnov	H2 a4 Cd9b1			
Brain	Kidnov	Efna3 Epha7	Colon	Kidnov	Gm7030 Cd9b1			
Brain	Brain	Efnad - Ephal	Kidney	Kidnov	Gm7030 - Cd8b1			
Kidnov	Hoart	Efnad Epha7	Colon	Hoart	H2 ag Cd4			
Kidnov	Colon	Efnañ Epha?	Colon	Hoart	H2 ab1 Cd4			
Kidnov	Broin	Efna5 Epha2	Colon	Hoart	H2 ob1 Cd4			
Livor	Brain	Effabl - Ephb2	Colon	Heart	H2 dma - Cd4			
Kidnov	Brain	Efab2 Ephod	Kidnov	Hoart	H2 dmb1 Cd4			
Hoart	Brain	Effeb2 Ephb2	Colon	Kidnov	H2 dmb2 Cd4			
Brain	Hoort	Effet2 - Epht2	Colon	Kidnov	H2 op Cd4			
Broin	Kidpov	Efeb2 Epbb2	Colon	Kidnov	H2-ob Cd4			
Kidnov	Hoart	Embz - Ephbs	Brain	Brain	Mozia Mozia			
Hoart	Kidpov	Icam1 - (Itgax+Itgb2)	Colon	Hoart	Noctin2 Tigit			
Kidnov	Liver	loam1 (Itgax+Itgb2)	Brain	Colon	Hibp1 (Kirk1+Hoet)			
Kidney	Kidner	leam1 - (itgal+itab2)	Boort	Liver	DIM - Notch1			
Musele	Liver	loam2 (itgal+ltgb2)	Broin	Hoart	lag1 Notch1			
Hoart	Hoort	loom1 (Itaom+Itab2)	brain Line and	Brain	Jag1 - Notch1			
Mucola	Liver	loam2 (Iteal±Iteb2)	riean.	Hoart	Jag1 - Notch2			
Kidnou	Liver	icani∠ - (iigai+iigozi)	Kidney	Musele	Jag1 - Notch2			
Riuney	Musel	Icanii - Spii	Noney	Heart	Jag1 - Notch4			
Brain	NUSCIE	10051 - 6020	Brain	neart Daoin	Jagz - Notch2			
Liver	Liver	ngb2 - C0226	Kidney	Brain	DILL - Notch2	_		



Figure S13. The immune microenvironment in each tissue analyzed by immune landscape analysis.