

Supplementary Materials

Table S1. Biometric parameters at sacrifice

	CONTROL		BC	
	FEMALE	MALE	FEMALE	MALE
Body weight (g)	11.9±0.37	13.7±0.53	11.1±0.35	12.5±0.17*
BAT weight (mg)	74.1±5.63	63.7±9.04	59.7±4.56	65.9±4.04
Inguinal WAT weight (mg)	167±5.15	149±14.27	138±19.94	125±9.30
Retroperitoneal WAT weight (mg)	27.8±2.82	23.1±2.77	18.3±1.58	18.2±0.83*
Gonadal WAT weight (mg)	59.1±2.30	129±15.8	59.2±10.9	102±3.06*
VAT/SAT ratio^a	0.52±0.04	1.03±0.07	0.59±0.15	0.99±0.07
Liver weight (mg)	703±42.4	736±43.2	619±8.91	645±60.4
Liver index^b	5.94±0.34	5.36±0.17	5.58±0.26	5.15±0.43

The offspring of Western diet-fed mouse dams was orally supplemented with placebo (control group) or beta-carotene (BC) from day 2 to day 21 of life and sacrificed at day 26 when tissues were sampled. BAT, brown adipose tissue; WAT, white adipose tissue; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; ^a ratio between VAT (gonadal plus retroperitoneal) and SAT (inguinal) depots mass; ^b liver weight expressed as a percentage of body weight. *, p<0.05, BC vs CONTROL, Student's *t*-test.

Table S2. Overlapping target genes in both sexes of miRNAs differentially expressed with neonatal beta-carotene (BC) supplementation in the liver of mouse offspring of Western diet-fed mothers and the DE miRNAs related to their regulation

Gene	MALE MICE		FEMALE MICE	
	miRNAs	Regulation by BC	miRNAs	Regulation by BC
Abhd13	mmu-miR-468-3p	Up	mmu-miR-320-3p	Down
Abtb1	mmu-miR-762	Up	mmu-miR-125b-5p*	Up
Adam22	mmu-miR-1967	Up	mmu-miR-182-5p	Down
Adamtsl3	mmu-miR-762	Up	mmu-miR-485-5p	Down
Agap1	mmu-miR-684	Up	mmu-miR-320-3p	Down
Arrb1	mmu-miR-762	Up	mmu-miR-133b-3p	Down
Asxl3	mmu-miR-684	Up	mmu-miR-182-5p mmu-miR-362-3p	Down Up
Atxn1	mmu-miR-684	Up	mmu-miR-103-3p mmu-miR-125a-5p mmu-miR-362-3p* mmu-miR-93-5p	Down Down Down Down
Blcap	mmu-miR-467a-5p mmu-miR-762	Up Up	mmu-miR-320-3p	Down
Bmerb1	mmu-miR-762	Up	mmu-miR-362-3p	Up
Btbd7	mmu-miR-467a-5p	Up	mmu-miR-93-5p	Up
Btrc	mmu-miR-762	Up	mmu-miR-103-3p	Up
Cacna1b	mmu-miR-762	Up	mmu-miR-133b-3p mmu-miR-125a-5p mmu-miR-125b-5p	Down Up Up
Cadm2	mmu-miR-468-3p mmu-miR-684	Up Up	mmu-miR-93-5p	Up
Celf1	mmu-miR-762	Up	mmu-miR-133b-3p	Down
Cers6	mmu-miR-1967	Up	mmu-miR-320-3p	Down
Cntn2	mmu-miR-762	Up	mmu-miR-668-3p	Down
Cplx3	mmu-miR-762	Up	mmu-miR-1968-5p	Down
Csnk1g1	mmu-miR-762	Up	mmu-miR-708-5p mmu-miR-93-5p	Down Up
Cux1	mmu-miR-1967 mmu-miR-467a-5p mmu-miR-684	Up Up Up	mmu-miR-133b-3p mmu-miR-320-3p	Down Down
Dab2ip	mmu-miR-762	Up	mmu-miR-182-5p	Down
Dazap2	mmu-miR-1967	Up	mmu-miR-125a-5p	Up
Dcun1d1	mmu-miR-1967	Up	mmu-miR-182-5p	Down
Dgcr8	mmu-miR-468-3p	Up	mmu-miR-103-3p	Up
Dync1li2	mmu-miR-467a-5p	Up	mmu-miR-182-5p mmu-miR-103-3p	Down Up
Egflam	mmu-miR-468-3p	Up	mmu-miR-103-3p	Up
Eif4a2	mmu-miR-762	Up	mmu-miR-103-3p	Up
Eif5a2	mmu-miR-467a-5p	Up	mmu-miR-125a-5p	Up
Emc10	mmu-miR-762	Up	mmu-miR-485-5p	Down
Enah	mmu-miR-684	Up	mmu-miR-224-5p	Down
Erc1	mmu-miR-762	Up	mmu-miR-93-5p	Up
Etv3	mmu-miR-1964-3p	Up	mmu-miR-103-3p	Up
Fam168a	mmu-miR-684	Up	mmu-miR-182-5p	Down
Fbxo41	mmu-miR-762	Up	mmu-miR-182-5p	Down
Foxp2	mmu-miR-762	Up	mmu-miR-182-5p	Down
Frmd8	mmu-miR-762	Up	mmu-miR-370-3p	Down

Fzd3	mmu-miR-762	Up	mmu-miR-320-3p	Down
Kalrn	mmu-miR-684	Up	mmu-miR-323-3p	Down
Kcnk10	mmu-miR-762	Up	mmu-miR-125a-5p mmu-miR-125b-5p mmu-miR-182-5p	Up Up Down
Kpna1	mmu-miR-684	Up	mmu-miR-103-3p	Up
Lhx6	mmu-miR-467a-5p mmu-miR-684*	Up Up	mmu-miR-93-5p	Up
Lin28b	mmu-miR-467a-5p	Up	mmu-miR-103-3p	Up
Mfap3l	mmu-miR-468-3p	Up	mmu-miR-93-5p	Up
Mktn1	mmu-miR-467a-5p	Up	mmu-miR-93-5p	Up
Myrf	mmu-miR-467a-5p	Up	mmu-miR-133b-3p	Down
Nav1	mmu-miR-1967*	Up	mmu-miR-103-3p	Up
Ndel1	mmu-miR-762	Up	mmu-miR-103-3p	Up
Nfib	mmu-miR-467a-5p mmu-miR-684	Up Up	mmu-miR-125a-5p	Up
Osbp16	mmu-miR-468-3p	Up	mmu-miR-103-3p	Up
Otud7b	mmu-miR-762	Up	mmu-miR-133b-3p mmu-miR-320-3p	Down Down
Pbx1	mmu-miR-1967	Up	mmu-miR-125a-5p	Up
Pik3r1	mmu-miR-762	Up	mmu-miR-320-3p mmu-miR-103-3p*	Down Up
Plagl1	mmu-miR-1967	Up	mmu-miR-125a-5p	Up
Ppp1r16b	mmu-miR-762	Up	mmu-miR-320-3p	Down
Prdm16	mmu-miR-467a-5p	Up	mmu-miR-182-5p	Down
Prlr	mmu-miR-1967	Up	mmu-miR-182-5p mmu-miR-485-5p	Down Down
Prr14l	mmu-miR-762	Up	mmu-miR-93-5p	Up
Rad18	mmu-miR-467a-5p	Up	mmu-miR-320-3p	Down
Retreg3	mmu-miR-1967	Up	mmu-miR-125a-5p	Up
Rora	mmu-miR-1967	Up	mmu-miR-103-3p mmu-miR-125b-5p mmu-miR-370-3p	Up Up Down
Runx1t1	mmu-miR-1967	Up	mmu-miR-133b-3p	Down
Sbno1	mmu-miR-1967	Up	mmu-miR-103-3p mmu-miR-125a-5p mmu-miR-125b-5p	Up Up Up
Slc6a17	mmu-miR-762	Up	mmu-miR-125a-5p mmu-miR-125b-5p	Up Up
Slc7a1	mmu-miR-762	Up	mmu-miR-122-5p*	Up
Slc8a1	mmu-miR-762	Up	mmu-miR-103-3p mmu-miR-362-3p	Up Up
Sntb2	mmu-miR-1967	Up	mmu-miR-93-5p	Up
Soga1	mmu-miR-762	Up	mmu-miR-320-3p	Down
St8sia2	mmu-miR-468-3p	Up	mmu-miR-485-5p	Down
Stard13	mmu-miR-684	Up	mmu-miR-182-5p	Down
Stum	mmu-miR-762	Up	mmu-miR-668-3p	Down
Suv39h1	mmu-miR-467a-5p	Up	mmu-miR-125a-5p	Up
Taf9b	mmu-miR-467a-5p	Up	mmu-miR-125b-5p	Up
Tnrc6b	mmu-miR-467a-5p	Up	mmu-miR-362-3p	Up
Trp53inp1	mmu-miR-468-3p	Up	mmu-miR-93-5p mmu-miR-125b-5p	Up Up
Trps1	mmu-miR-684	Up	mmu-miR-125a-5p	Up
Tspan18	mmu-miR-762	Up	mmu-miR-485-5p	Down
Ube2l3	mmu-miR-762	Up	mmu-miR-125b-5p	Up

Ubn2	mmu-miR-684	Up	mmu-miR-224-5p mmu-miR-320-3p	Down Down
Ubxn2b	mmu-miR-468-3p	Up	mmu-miR-93-5p	Up
Usf3	mmu-miR-684	Up	mmu-miR-122-5p	Up
Xpo7	mmu-miR-762*	Up	mmu-miR-668-3p	Down
Zbtb37	mmu-miR-467a-5p	Up	mmu-miR-182-5p	Down
Zc3h12c	mmu-miR-467a-5p mmu-miR-468-3p	Up Up	mmu-miR-93-5p mmu-miR-103-3p	Up Up
Zfp174	mmu-miR-762	Up	mmu-miR-224-5p	Down
Zfp704	mmu-miR-684	Up	mmu-miR-182-5p	Down
Znrf3	mmu-miR-467a-5p	Up	mmu-miR-125a-5p mmu-miR-133b-3p	Up Down

*Bold highlight indicates the miRNAs validated for the gene.

Table S3. KEGG pathway adscriptions of overlapping target genes in both sexes of miRNAs differentially expressed with neonatal beta-carotene supplementation in the liver of mouse offspring of Western diet-fed mothers

FEMALE MICE- target-miRNA downregulated		
ID pathway	Pathways	Gene
mmu05207	Chemical carcinogenesis - receptor activation	Cacna1b, Pik3r1, Arrb1,
mmu05205	Proteoglycans in cancer	Pik3r1, Fdz3
mmu04010	MAPK signaling pathway	Cacna1b, Arrb1
mmu04810	Regulation of actin cytoskeleton	Enah,
mmu04360	Axon guidance	Enah, Pik3r1, Fdz3,
mmu05211	Renal cell carcinoma	Pik3r1
mmu04015	Rap1 signaling pathway	Enah,Pik3r1
mmu05223	Non-small cell lung cancer	Pik3r1
mmu04062	Chemokine signaling pathway	Pik3r1, Arrb1
mmu04510	Focal adhesion	Pik3r1
mmu04071	Sphingolipid signaling pathway	Cers6, Pik3r1
mmu04550	Signaling pathways regulating pluripotency of stem cells	Pik3r1, Fdz3
mmu04666	Fc gamma R-mediated phagocytosis	Pik3r1
mmu05218	Melanoma	Pik3r1
mmu04722	Neurotrophin signaling pathway	Pik3r1
mmu05212	Pancreatic cancer	Pik3r1
mmu05220	Chronic myeloid leukemia	Pik3r1
mmu04144	Endocytosis	Agap1, Arrb1
mmu04068	FoxO signaling pathway	Pik3r1
mmu04012	ErbB signaling pathway	Pik3r1
mmu04211	Longevity regulating pathway	Pik3r1
mmu05225	Hepatocellular carcinoma	Pik3r1, fdz3
mmu04670	Leukocyte transendothelial migration	Pik3r1
mmu05226	Gastric cancer	Pik3r1, fdz3
mmu05221	Acute myeloid leukemia	Pik3r1, Runx1t1
mmu04070	Phosphatidylinositol signaling system	Pik3r1
mmu04611	Platelet activation	Pik3r1
mmu05417	Lipid and atherosclerosis	Pik3r1
mmu04390	Hippo signaling pathway	Fzd3
mmu04917	Prolactin signaling pathway	Prlr, Pik3r1
mmu04024	cAMP signaling pathway	Pik3r1
mmu04660	T cell receptor signaling pathway	Pik3r1
mmu04934	Cushing syndrome	Fdz3
mmu01521	EGFR tyrosine kinase inhibitor resistance	Pik3r1
mmu00600	Sphingolipid metabolism	Cers6
mmu05017	Spinocerebellar ataxia	Pik3r1, Rora
mmu04923	Regulation of lipolysis in adipocytes	Pik3r1
mmu04140	Autophagy - animal	Pik3r1
mmu04340	Hedgehog signaling pathway	Csnk1g1, Arrb1
mmu05213	Endometrial cancer	Pik3r1
mmu05224	Breast cancer	Pik3r1, Fdz3
mmu03013	Nucleocytoplasmic transport	Xpo7
mmu04935	Growth hormone synthesis, secretion and action	Pik3r1
mmu05210	Colorectal cancer	Pik3r1
mmu04213	Longevity regulating pathway - multiple species	Pik3r1
FEMALE MICE- target-miRNA upregulated		
mmu04330	Notch signaling pathway	Atxn1,
mmu04710	Circadian rhythm	Rora, Btrc

mmu05223	Non-small cell lung cancer	Pik3r1
mmu01522	Endocrine resistance	Pik3r1
mmu05222	Small cell lung cancer	Pik3r1
mmu05220	Chronic myeloid leukemia	Pik3r1
mmu04340	Hedgehog signaling pathway	Btrc
mmu05224	Breast cancer	Pik3r1
mmu05207	Chemical carcinogenesis - receptor activation	Cacna1b, Kpna1, Pik3r1
mmu04218	Cellular senescence	Btrc, Pik3r1
mmu04668	TNF signaling pathway	Pik3r1
mmu04140	Autophagy - animal	Pik3r1
mmu04917	Prolactin signaling pathway	Pik3r1
mmu05214	Glioma	Pik3r1
mmu04310	Wnt signaling pathway	Btrc, Znf3
mmu05212	Pancreatic cancer	Pik3r1
mmu05215	Prostate cancer	Pik3r1
mmu05169	Epstein-Barr virus infection	Pik3r1
mmu05226	Gastric cancer	Pik3r1
mmu04152	AMPK signaling pathway	Pik3r1
mmu05165	Human papillomavirus infection	Pik3r1
mmu04390	Hippo signaling pathway	Btrc
mmu05206	MicroRNAs in cancer	Pik3r1
mmu05161	Hepatitis B	Pik3r1
mmu05160	Hepatitis C	Pik3r1
mmu04550	Signaling pathways regulating pluripotency of stem cells	Pik3r1
mmu05167	Kaposi sarcoma-associated herpesvirus infection	Pik3r1
mmu05410	Hypertrophic cardiomyopathy	Slc8a1, Pik3r1
mmu05225	Hepatocellular carcinoma	Pik3r1
mmu05218	Melanoma	Pik3r1
mmu05412	Arrhythmogenic right ventricular cardiomyopathy	Slc8a1
mmu04370	VEGF signaling pathway	Pik3r1
mmu04010	MAPK signaling pathway	Cacna1b
mmu04066	HIF-1 signaling pathway	Pik3r1
mmu05022	Pathways of neurodegeneration - multiple diseases	Cacna1b, Atxn1
mmu05162	Measles	Pik3r1
mmu05211	Renal cell carcinoma	Pik3r1
mmu05414	Dilated cardiomyopathy	Slc8a1
mmu04071	Sphingolipid signaling pathway	Pik3r1
mmu04068	FoxO signaling pathway	Pik3r1
mmu04978	Mineral absorption	Slc8a1
mmu05017	Spinocerebellar ataxia	Atxn1, Rora, Pik3r1
mmu04935	Growth hormone synthesis, secretion and action	Pik3r1
mmu05210	Colorectal cancer	Pik3r1
mmu04360	Axon guidance	Pik3r1
mmu04961	Endocrine and other factor-regulated calcium reabsorption	Slc8a1
mmu04261	Adrenergic signaling in cardiomyocytes	Slc8a1,
mmu04722	Neurotrophin signaling pathway	Pik3r1
mmu05163	Human cytomegalovirus infection	Pik3r1
MALE MICE- target-miRNA upregulated		
mmu04360	Axon guidance	Enah, Pik3r1, Fdz3
mmu04514	Cell adhesion molecules	Cntn2
mmu04728	Dopaminergic synapse	Cacna1b, arrb1
mmu04926	Relaxin signaling pathway	Pik3r1, arrb1
mmu04340	Hedgehog signaling pathway	Btrc, arrb1
mmu04012	ErbB signaling pathway	Pik3r1

mmu04931	Insulin resistance	Pik3r1
mmu05170	Human immunodeficiency virus 1 infection	Btrc, Pik3r1
mmu04725	Cholinergic synapse	Cacna1b, Pik3r1
mmu04015	Rap1 signaling pathway	Enah, Pik3r1
mmu05032	Morphine addiction	Cacna1b, Arrb1
mmu04670	Leukocyte transendothelial migration	Pik3r1
mmu05132	Salmonella infection	Kpna1, Dync1li2
mmu04710	Circadian rhythm	Rora, Btrc
mmu00600	Sphingolipid metabolism	Cers6
mmu04010	MAPK signaling pathway	Cacna1b, arrb1
mmu04660	T cell receptor signaling pathway	Pik3r1
mmu05142	Chagas disease	Pik3r1
mmu04151	PI3K-Akt signaling pathway	Prlr, Pik3r1
mmu05165	Human papillomavirus infection	Pik3r1
mmu04928	Parathyroid hormone synthesis, secretion and action	Arrb1
mmu04371	Apelin signaling pathway	Slc8a1,
mmu04668	TNF signaling pathway	Pik3r1, Dab2ip
mmu04727	GABAergic synapse	Cacna1b
mmu05207	Chemical carcinogenesis - receptor activation	Cacna1b, Pik3r1, Kpna1, Arrb1
mmu04935	Growth hormone synthesis, secretion and action	Pik3r1
mmu04810	Regulation of actin cytoskeleton	Enah, pik3r1
mmu01522	Endocrine resistance	pik3r1
mmu05418	Fluid shear stress and atherosclerosis	pik3r1,
mmu04723	Retrograde endocannabinoid signaling	Cacna1b
mmu04722	Neurotrophin signaling pathway	Pik3r1
mmu04014	Ras signaling pathway	Pik3r1
mmu04930	Type II diabetes mellitus	Cacna1b, Pik3r1
mmu04071	Sphingolipid signaling pathway	Cers6, Pik3r1,
mmu05231	Choline metabolism in cancer	Pik3r1
mmu04917	Prolactin signaling pathway	Prlr, Pik3r1
mmu04721	Synaptic vesicle cycle	Cacna1b
mmu04978	Mineral absorption	Slc8a1
mmu04915	Estrogen signaling pathway	Pik3r1
mmu05160	Hepatitis C	Pik3r1

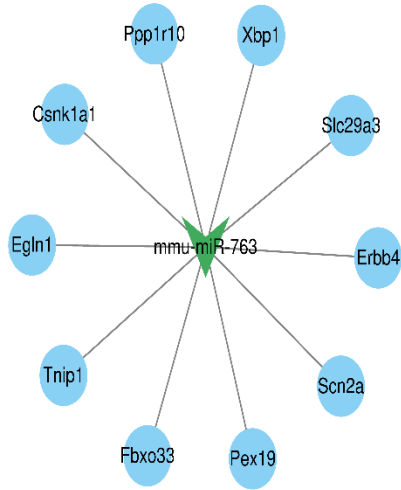
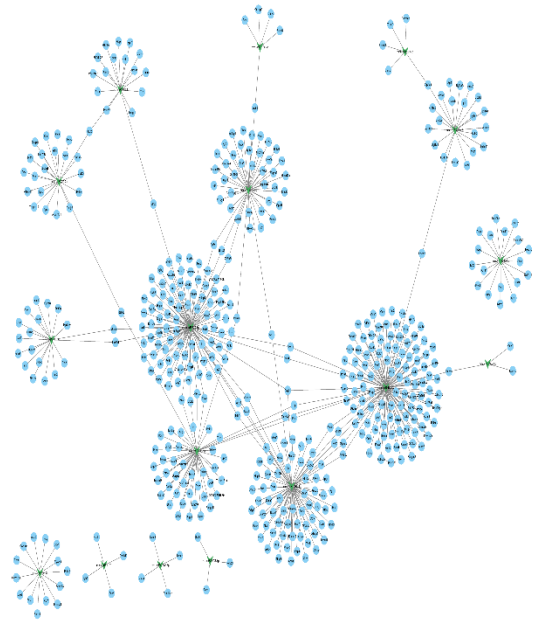
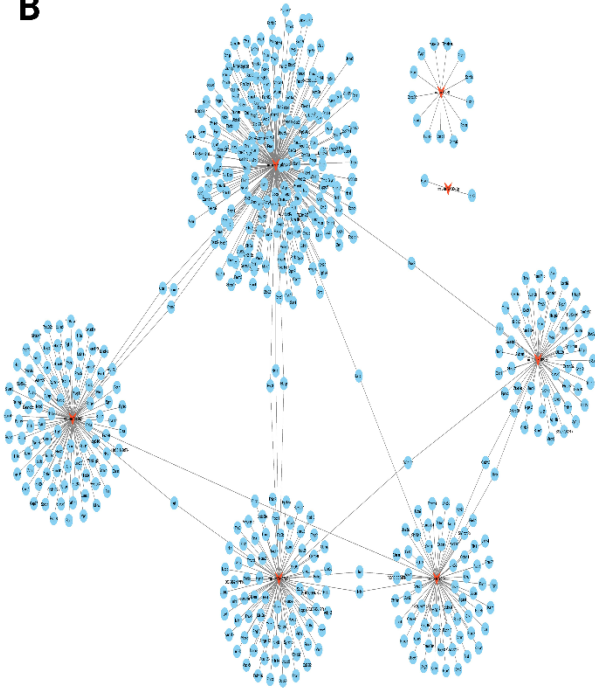
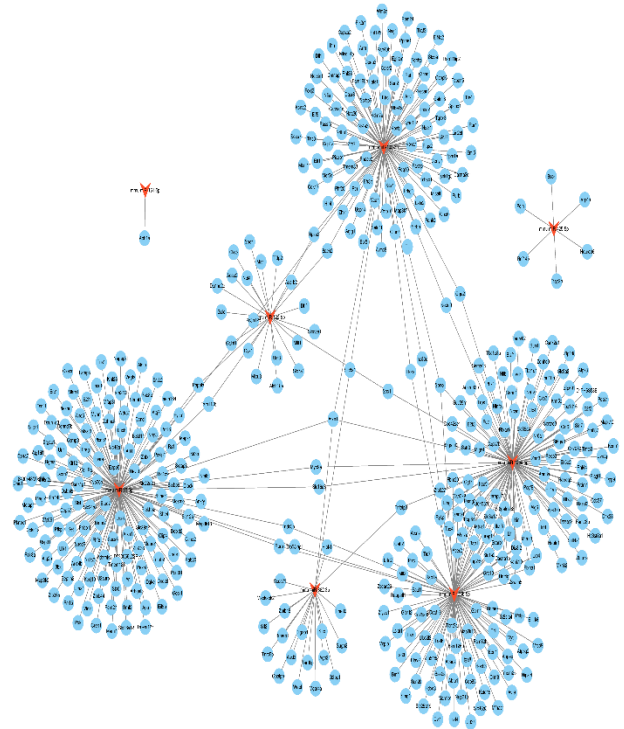
A**C****B****D**

Figure S1. miRNA-gene interaction networks. The miRNAs found to be differentially expressed with neonatal beta-carotene (BC) supplementation in the liver of mice born from Western diet- fed dams and their predicted gene targets are illustrated as networks. Each individual node represents a miRNA or gene. **Networks are for: A)** The only miRNA found to be significantly downregulated in BC males **B)** Upregulated miRNAs in BC males **C)** Downregulated miRNAs in BC females **D)** Upregulated miRNAs in BC females.

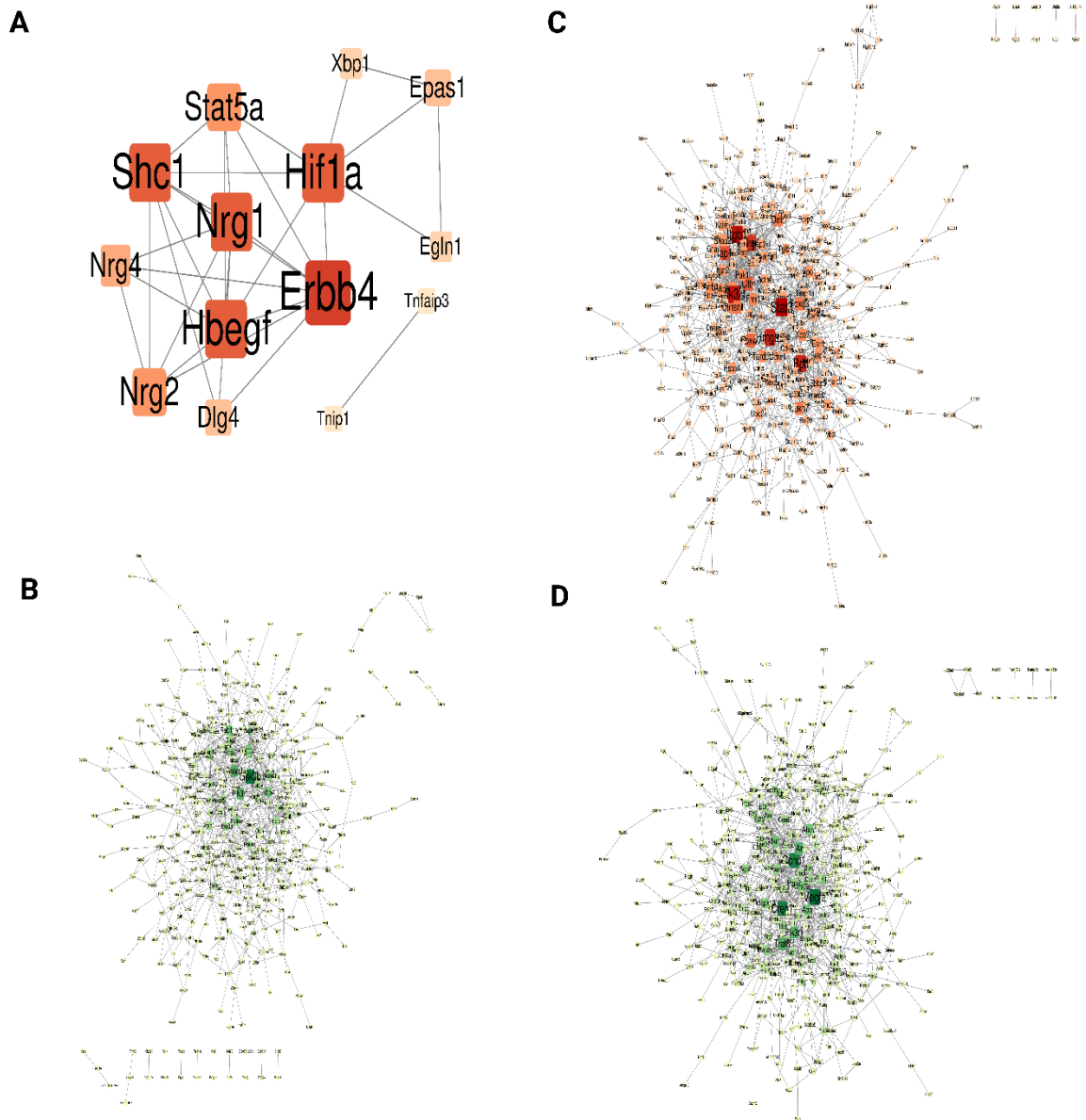


Figure S2. Protein-protein interaction (PPI) networks of predicted targets of the miRNAs differentially expressed with neonatal beta-carotene (BC) supplementation in the liver of offspring of Western diet-fed mouse dams. Each node is a protein, and an edge is an interaction between two proteins. **A)** PPI of the downregulated miRNA targets in BC males **B)** PPI of upregulated miRNA targets in BC males **C)** PPI of downregulated miRNA targets in BC females **D)** PPI of upregulated miRNA targets in BC females.