

Supplemental Tables

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Supplemental Table 1. Drugs and recombinant proteins

Drugs and Recombinant Proteins	Final Concentration Used	Source
Glucose	30 mmol/L	Sigma G5500
Mannitol	24.4 mmol/L	Sigma M-9546
Recombinant mouse TGF β 1	0.5ng/ml	R&D Systems 7666-MB
Recombinant mouse Follistatin-288	500ng/ml	R&D system 769-FS
Recombinant human cripto-1	0.5-1 μ g/ml	Biolegend 777804
Recombinant mouse activin A	1 or 5ng/ml	R&D Systems 338-AC
TGF β 1 neutralizing antibody 1D11	1 μ g/ml	R&D Systems MAB1835
Activin B neutralizing antibody	3 μ g/ml	R&D Systems MAB659
Activin A neutralizing antibody	3.5 μ g/ml	R&D Systems MAB3381

Supplemental Table 2. qPCR Primers

Primer	Forward	Reverse
mmu-miR-299a-5p	TGGTTTACCGTCCCACATACAT	Universal – Proprietary (Quanta)
Mouse 18S rRNA	GCCGCTAGAGGTGAAATTCTTG	CATTCTTGGCAAATGCTTTCG
Mouse cripto-1	TGTTGCGAAAGAGCACTGTGG	TGAGGTCCTGGTCCATCACTTGAC

Supplemental Table 3. miR LNA anti-miR probes for ISH and *in vivo* inhibition

	Application	Concentration	Source
5'/3' DIG mmu-miR-299a-5p miRCURY LNA detection probe	ISH	10pmol	Exiqon/Qiagen; YD00615334
5' DIG U6 miRCURY LNA detection probe, positive control	ISH	10pmol	Exiqon/Qiagen; YD00699002
<i>In vivo</i> LNA anti-miR Inhibitor targeting mmu-miR-299a-5p	Mice Treatment (IP)	2mg/kg (weekly for 12 weeks)	Exiqon/Qiagen; 339204
<i>In vivo</i> LNA anti-miR Inhibitor Negative Control "B"	Mice Treatment (IP)	2mg/kg (weekly for 12 weeks)	Exiqon/Qiagen; 339204

Supplemental Table 4. Plasmids

Construct	Source
CAGA12 Luciferase	Dr. Marie Bilandzic, Prince Henry's Institute, Australia
Coll α 1 Luciferase	Dr. Vincent Falanga, University of Miami, USA
miR-299a-5p MRE-Luc	Constructed in the lab ⁵
miR-299a-5p precursor clone (GFP)	Genecopoeia; MmiR3388-MR04
miRNA scrambled precursor control clone (GFP)	Genecopoeia; CmiR0001-MR04
miR-299a-5p inhibitor clone (mCherry)	Genecopoeia; MmiR-AN0369-AM02
miRNA inhibitor scrambled control clone (mCherry)	Genecopoeia; CmiR-AN0001-AM02
miRNA 3'UTR target expression clone for Mouse Cripto-1	Genecopoeia; MmiT030329-MT06
miRNA Target clone control vector for pEZX-MT06	Genecopoeia; CmiT000001-MT06

Supplemental Table 5. Antibodies

Antibody	Application	Concentration	Source
anti-Digoxigenin-AP Fab fragment	ISH	1:500	Sigma Aldrich; 11093274910
Activin A	IHC	1:100 30min citric acid steam for IHC antigen retrieval	ProteinTech; 10651-1-AP
Collagen 1 α 1	WB	1:10,000	Abcam; ab84956
Collagen IV α 1	IHC	1:200 30min citric acid steam for IHC antigen retrieval	Novus; NB120-6586SS
Cripto-1	WB	1:1000	Rockland; 600-401-997S
CTGF	WB, IHC	1:2000, 1:75 30min citric acid steam for IHC antigen retrieval	Santa Cruz; sc-34772
Follistatin	IHC	1:500 30min citric acid steam for IHC antigen retrieval	LSBIO; LS-B14665
Follistatin (H-114)	WB	1:500	Santa Cruz; sc-30194
Fibronectin	WB, IHC	1:1000; 1:500 Antigen retrieval for 40 μ g proteinase K for IHC antigen retrieval	BD Transduction 610078; Sigma F3648
GAPDH	WB	1:100,000	Cell Signaling Technology; 2118
Nephrin	IF	1:10,000	R&D; AF3159
Phospho-SMAD3	WB	1:2000	Novus; NBP1-77836
Total SMAD3	WB	1:2000	Abcam; ab-40854

Supplemental Table 6. Clinical characteristics of mice

	HH-LNac	HH-LNAi	HH-A-LNac	HH-A-LNAi
Fasted Blood Glucose (mmol/L)	9.3± 0.7	9.3 ± 0.5	31.5 ± 1.7 ***	31.9 ± 0.5 ⁺
Endpoint Weight (g)	37.0 ± 1.3	34.2 ± 1.6	30.1 ± 0.7 **	28.2 ± 0.6 [#]

Data presented as mean ± SEM. Significance between HH-LNac and HH-A-LNac groups are represented as **p<0.01, ***p<0.0001. Significance HH-LNAi and HH-A-LNAi groups are represented as #p<0.01, +p<0.0001.

Supplemental Table 7. Blood pressure

	HH-LNac	HH-LNAi	HH-A-LNac	HH-A-LNAi
Baseline (enrollment) SBP (mmHg)	130.7 ± 3.3	130.2 ± 1.2	151.1 ± 2.7 ^{***, @}	149.4 ± 2.8 ^{&, ^}
Baseline (enrollment) DBP (mmHg)	101.2 ± 3.6	98.6 ± 1.5	116.3 ± 2.7 ^{*, %}	114.8 ± 3.8 ^{&, \$\$}
4-week SBP (mmHg)	133.8 ± 4.7	133 ± 4.2	154.3 ± 2.8 ^{***, @}	145.2 ± 2.1
4-week DBP (mmHg)	106.4 ± 4.4	104.6 ± 4.2	122.7 ± 2.6 ^{**, %}	110.7 ± 2.2 ^{\$\$\$}
8-week SBP (mmHg)	135.1 ± 2.9	129.8 ± 3.7	152.2 ± 3.1 ^{**, @}	143.6 ± 4.6 ⁺
8-week DBP (mmHg)	107 ± 1.6	102.5 ± 3.3	119.98 ± 3.5 ^{*, %}	108.6 ± 3.5 ^{\$\$\$}
12-week SBP (mmHg)	133.3 ± 4.7	127.9 ± 3.5	159.5 ± 3.6 ^{***, @}	146 ± 3.3 ^{&, \$\$\$}
12-week DBP (mmHg)	103.7 ± 5.1	99.15 ± 2.2	128 ± 2.8 ^{***, @}	111.4 ± 4.1 ^{##}

SBP=systolic blood pressure; DBP=diastolic blood pressure, data presented as mean ± SEM.

Significance between HH-LNac and HH-A-LNac groups are represented as *p< 0.05,

p<0.01, *p<0.0001. Significance between HH-LNAi and HH-A-LNAi groups are

represented as +p<0.05, &p<0.01. Significance between HH-LNAi and HH-A-LNac groups are

represented as %p<0.01, @p<0.0001. Significance between HH-LNac and HH-A-LNAi groups

are represented as \$\$p<0.05, ^p<0.01. Significance between HH-A-LNac and HH-A-LNAi

groups are represented as \$\$\$p<0.05, ##p<0.001.