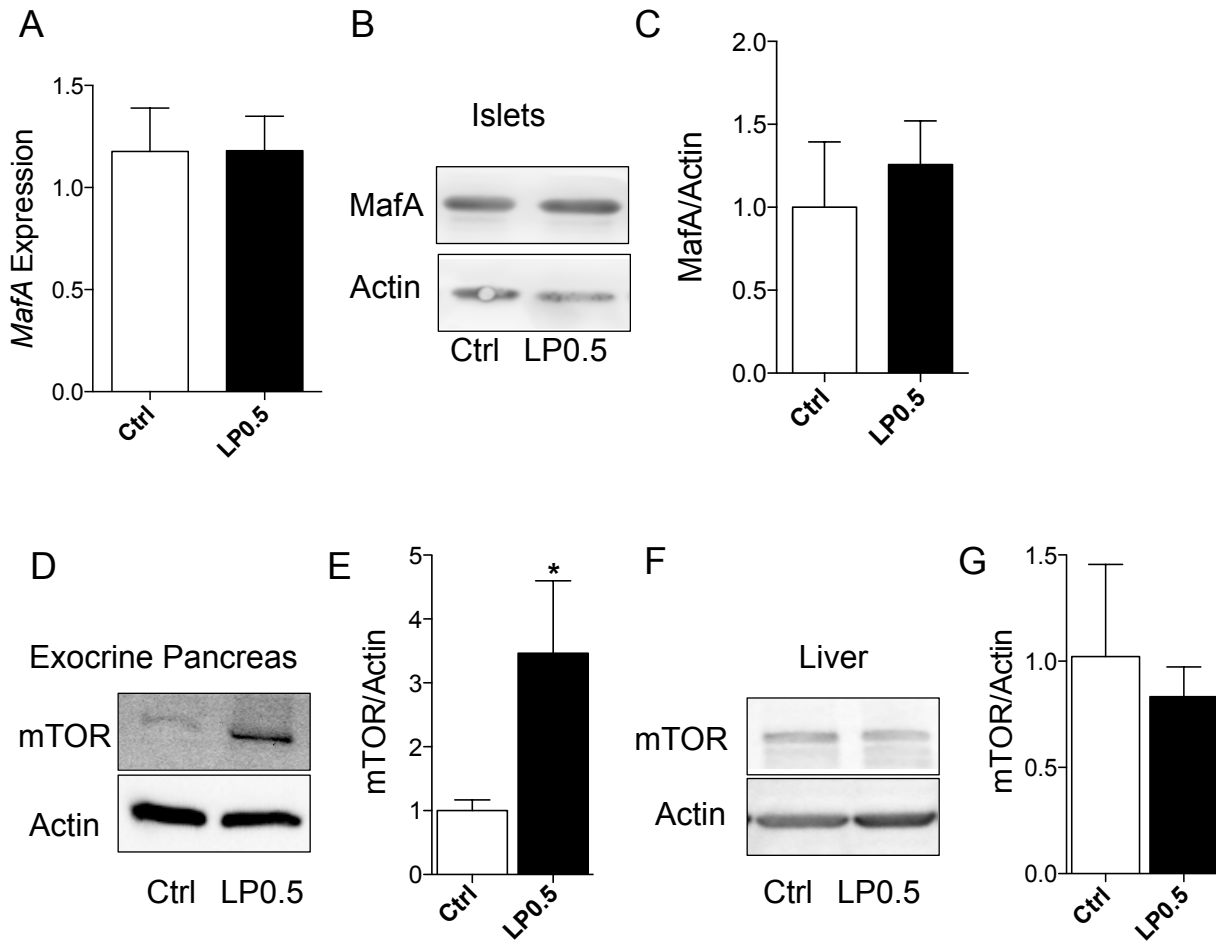
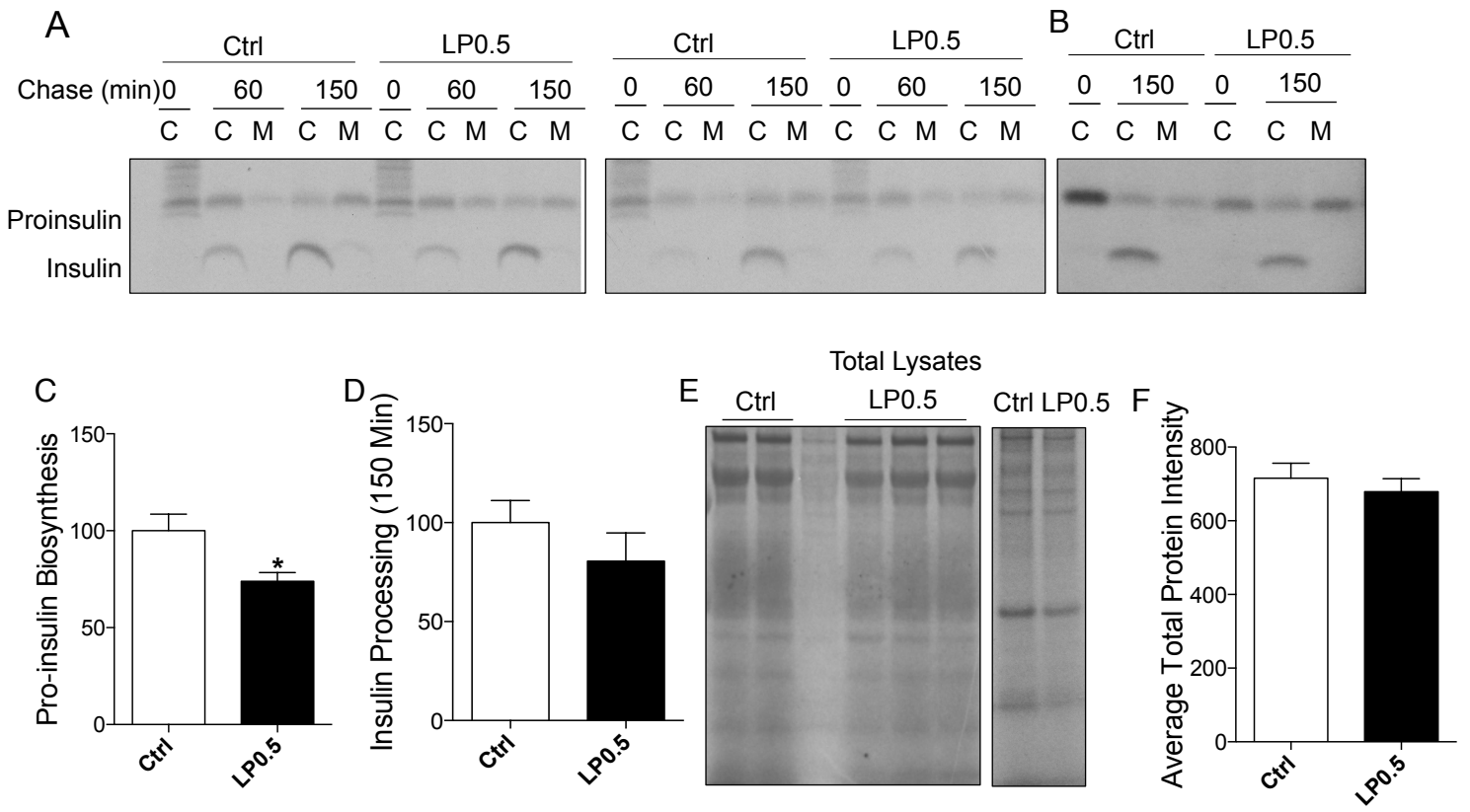


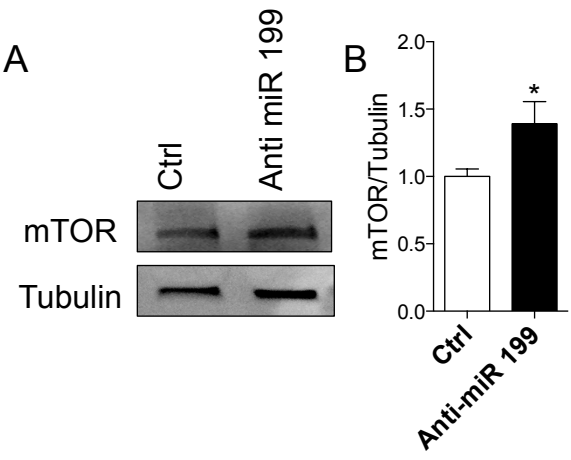
# Supplemental Figure 1



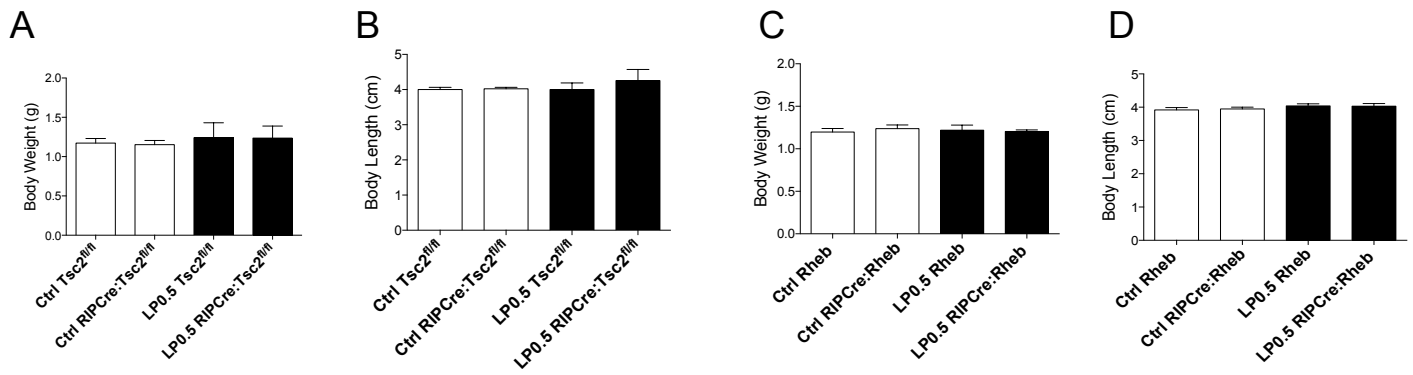
# Supplemental Figure 2



Supplemental Figure 3



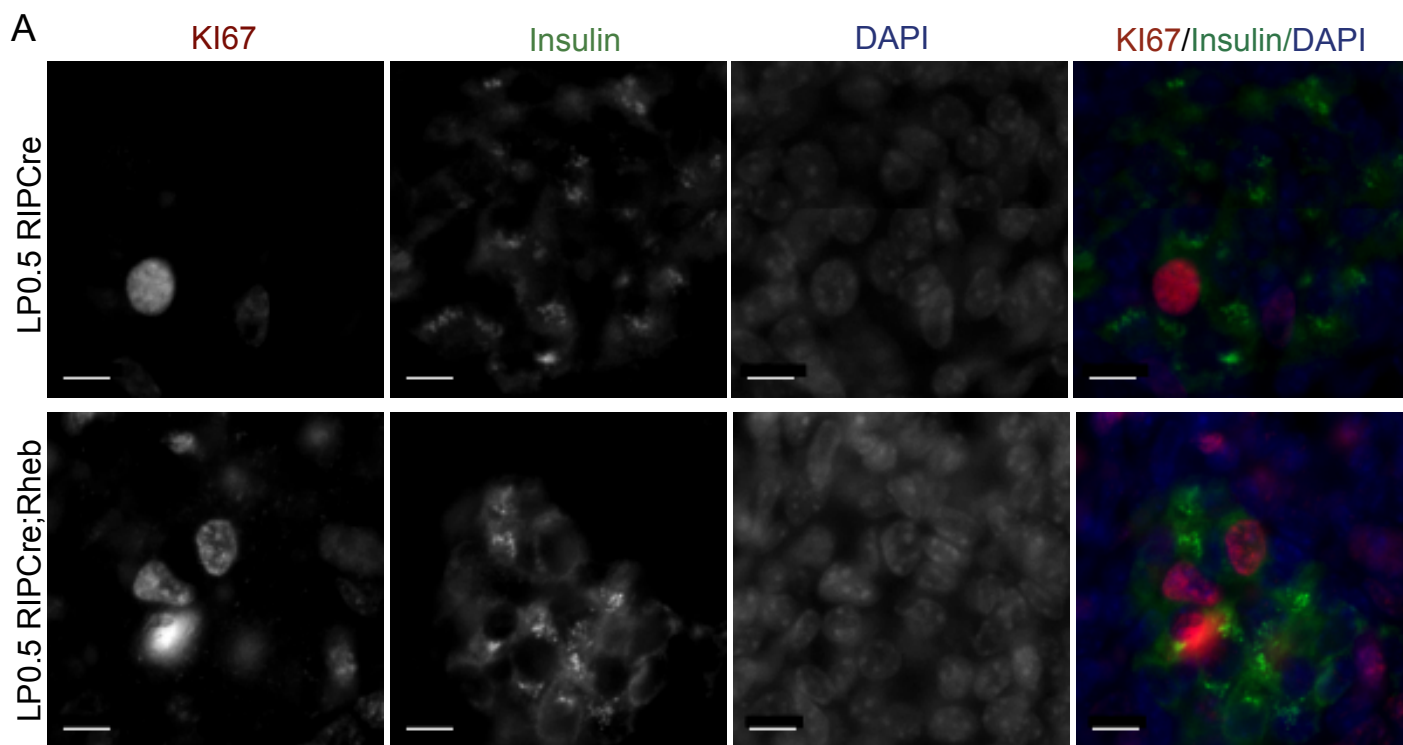
## Supplemental Figure 4



### Supplemental Figure 4. Phenotype of newborn mice harboring either a *Tsc2* deletion or *Rheb*-overexpression specifically in $\beta$ -cells.

(A-B) Body weight or length of wildtype *Tsc2<sup>fl/fl</sup>* Ctrl or LP0.5 and *RIPCre;Tsc2<sup>fl/fl</sup>* Ctrl or LP0.5 newborn. (C-D) Body weight or length of wildtype *RIPCre* Ctrl or LP0.5 and *RIPCre;Rheb* Ctrl or LP0.5 newborn. n=3-7 for *Tsc2* cohort and n=4-7 for *Rheb* cohort.

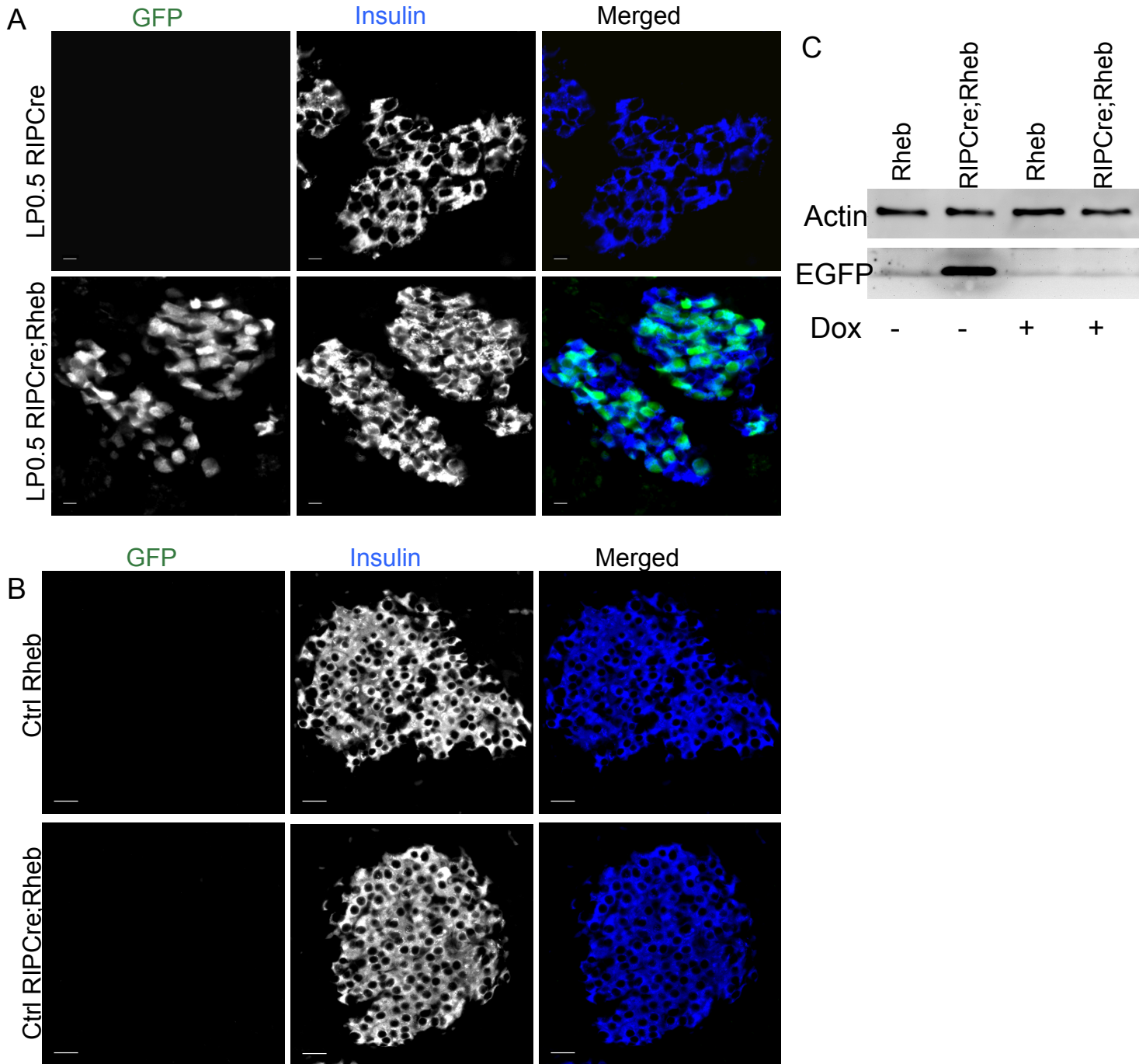
## Supplemental Figure 5



**Supplemental Figure 5. Enhanced proliferation in LP0.5 mice overexpressing Rheb(RIPCre;Rheb) in  $\beta$ -cells.**

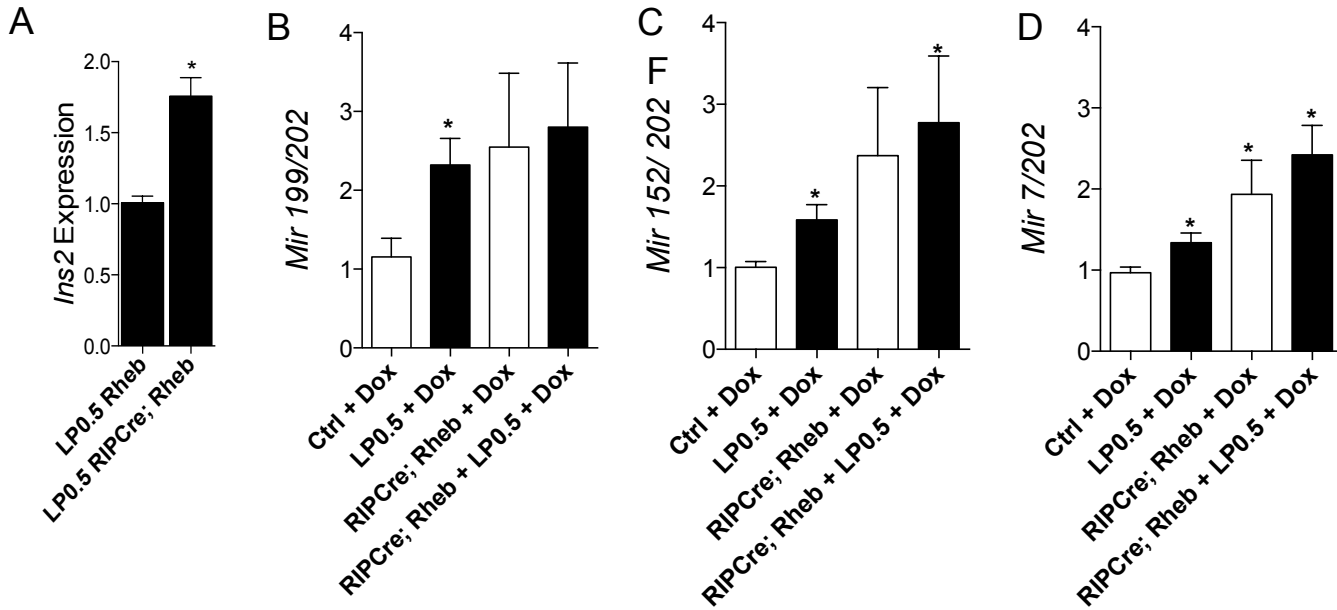
**(A)** Proliferation measured by KI67 (red) in insulin-producing cells (green) from islets of LP0.5 mice overexpressing Rheb (*RIPCre;Rheb*) or wild type (*RIPCre*). Scale bar is 100  $\mu$ m.

Supplemental Figure 6



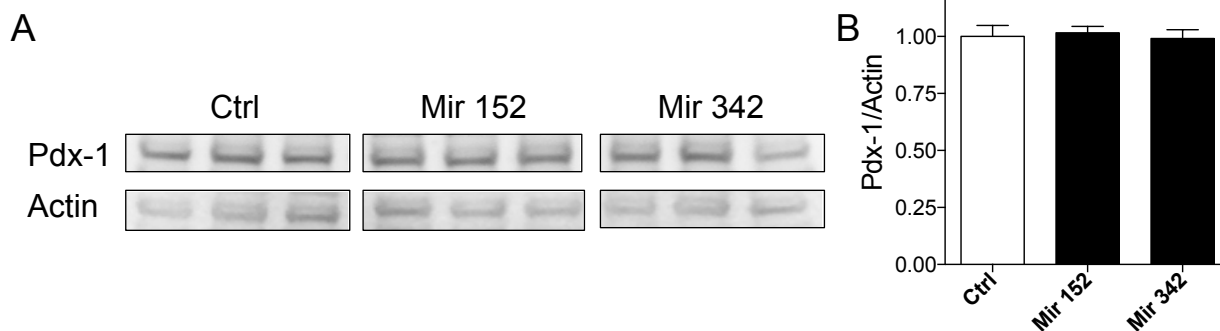
**Supplemental Figure 6. Characterization of islets from *RIPCre;Rheb* mice. (A)** Specific expression of EGFP (Green) in insulin-producing cells (Blue) of LP0.5 offspring overexpressing Rheb (*RIPCre;Rheb*) or wild type (*RIPCre*). Scale bar is 20  $\mu$ m. **(B)** EGFP in control offspring with overexpressing Rheb (*RIPCre;Rheb*) or wild type (*RIPCre*) exposed to Dox throughout life. Scale bar is 100  $\mu$ m. **(C)** Immunoblotting of EGFP in islets isolated from either *RIPCre;Rheb* or *Rheb* mice with or without Dox treatment.

## Supplemental Figure 7



**Supplemental Figure 7. MicroRNAs expression in *RIPCre;Rheb* mice. (A)** *Insulin 2* transcription message from islets of male LP0.5 *Rheb* and LP0.5 *RIPCre;Rheb* mice. **(B-D)** MicroRNAs (miRs) expression in islets from *Rheb* and *RIPCre;Rheb* in Ctrl or LP0.5 diet with Dox after birth to death, n=3. \* $P < 0.05$  vs. Ctrl.

## Supplemental Figure 8



**Supplemental Figure 8. Pdx-1 protein level is not altered in INS-1 cells treated with mimic miR 152 and miR 342.** (A) Pdx-1 protein levels in INS-1 cells treated with mimic miRs 152 and 342 for 24hr. (B) Quantification of Pdx-1 protein corrected to actin, n=3. \*P < 0.05 vs. Ctrl.



## Supplemental Table 1

	Ctrl		LP0.5	
	gm%	kcal%	gm%	kcal%
Protein	22.7	23.5	9.3	9.6
Carbohydrate	64.0	66.3	77.4	80.2
Fat	4.4	10.2	4.4	10.2
Total	91.1	100.0	91.1	100.0
kcal/gm	3.86		3.86	
<b>Ingredient</b>	<b>gm</b>	<b>kcal</b>	<b>gm</b>	<b>kcal</b>
Casein	220	880	90	360
DL-Methionine	2	8	0.8	3.2
Corn Starch	80	320	80	320
Dextrose	536.5	2146	667.8	2671.2
Cellulose, BW200	50	0	50	0
Soybean Oil	43	387	43	387
Mineral Mix S10001	35	0	35	0
Vitamin Mix V10001	10	40	10	40
Choline Bitartrate	2	0	2	0
FD&C Red Dye #40	0	0	0.05	0
FD&C Yellow Dye #5	0.025	0	0	0
FD&C Blue Dye #1	0.025	0	0	0
<b>Total</b>	<b>978.55</b>	<b>3781</b>	<b>978.65</b>	<b>3781</b>

**Supplemental Table 1. Diet composition used in the maternal low-protein diet model.** Isocaloric low-protein (9%, D02041002,) or ctrl diet (23% D02041001B) were purchased from Research Diets Inc.

## Supplemental Table 2

<b>Gene</b>	<b>Left</b>	<b>Right</b>
<i>Gck</i>	cacaaatgctcccagcca	ccatttccaggggtagca
<i>Hnf1<math>\alpha</math></i>	cgctccaccctgggtat	actccccatgctgtgatg
<i>Hnf4<math>\alpha</math></i>	ccaagaggtccatggtgtt	ccgagggacgatgtagcat
<i>Ins1</i>	gccatggtgaaacaatgacct	cagagaggaaggtactttggactataa
<i>Ins2</i>	gaagtggaggaccacaagt	agtccaaggtctgaaggtc
<i>Igf2</i>	cgcttcagttgtctgttcg	gcagcactctccacgatg
<i>Neurod1</i>	cgcagaaggcaagggtgc	ttggatcatgttccactcc
<i>Tcf2 (Hfn1<math>\beta</math>)</i>	ggtgtagcgcactcctga	atggctcccctcaccate
<i>Pdx1</i>	gaaatccaccaagctcacg	cgggttccgctgtgtaag
<i>Mtor</i>	agaagacagcggggaagg	gcacttgcctgaggttc

**Supplemental Table 2.** These primers were designed by ProbeFinder and were optimized for real-time PCR Assay for the listed mRNA.