
بسم الله الرحمن الرحیم

Micro RNA and Diabetes

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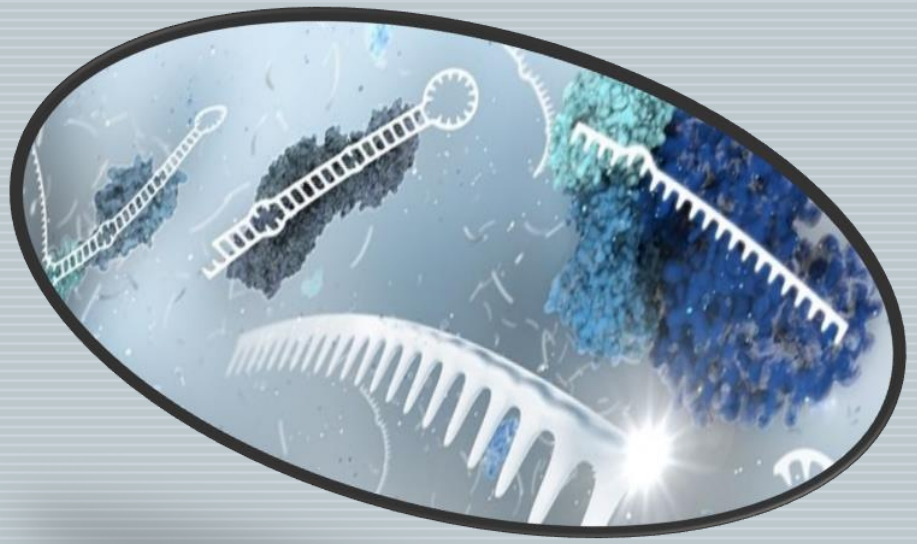
content

- Introduction of miRNA
- Biogenesis of miRNA
- Diabetes
- Communication miRNA and diabetes and Complication of diabetes
- Communication Drugs of Antidiabetic and miRNA

MiRNA

Definition:

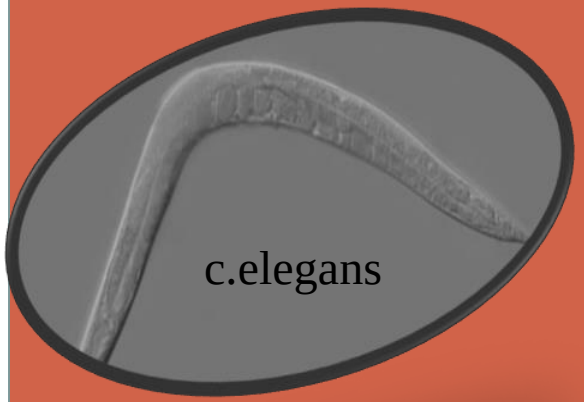
- Small (20-22 nt)
- Non coding
- Single-strand
- Endogenous RNA



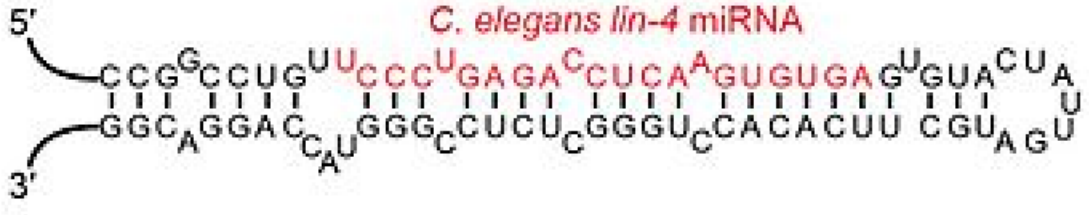
MiRNA

History:

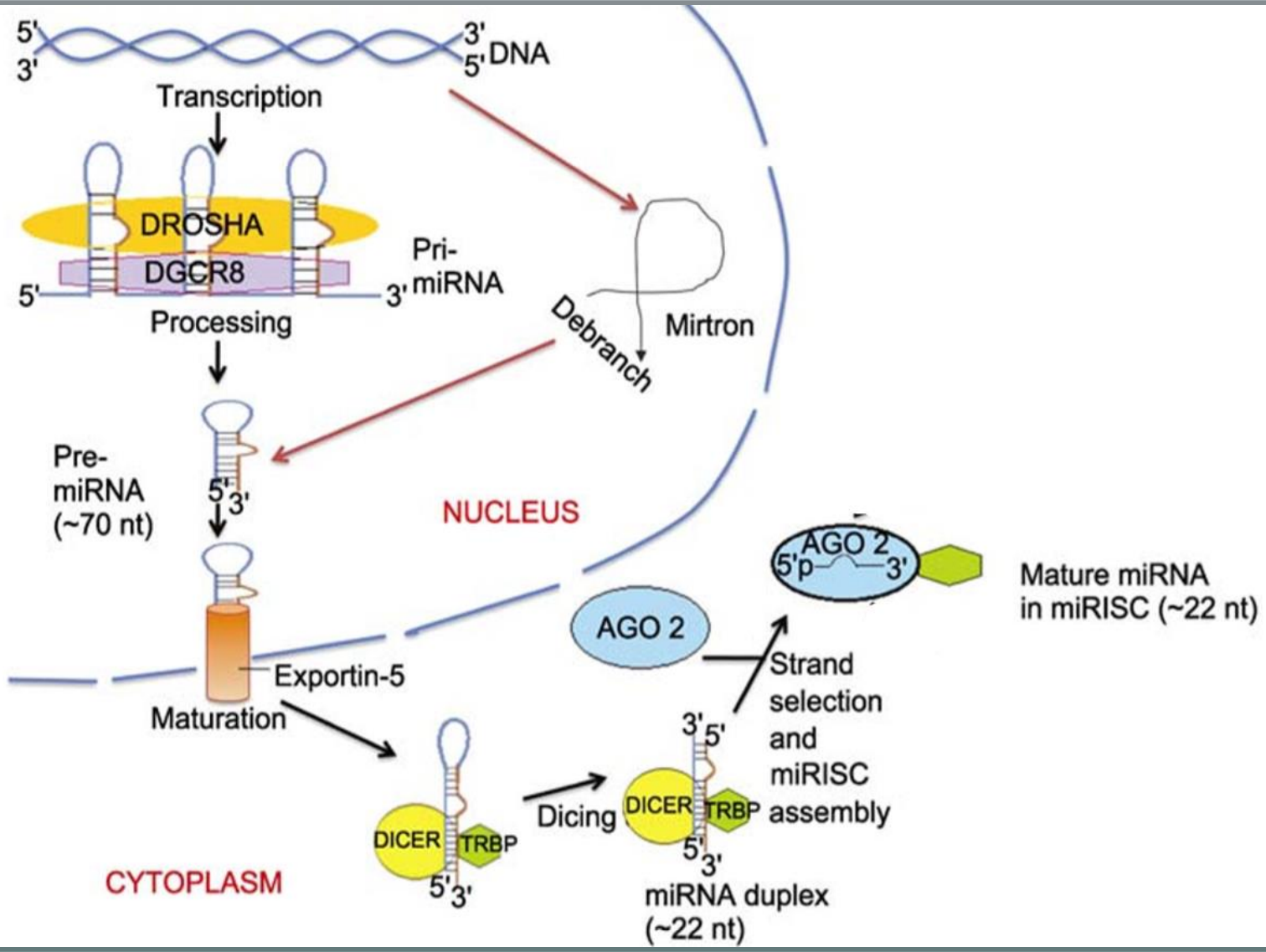
- First miRNA ⟶ lin-4
- By Lee & Ambrose in 1993
- Nematode: C. elegans
- Human,plant,virus



c.elegans

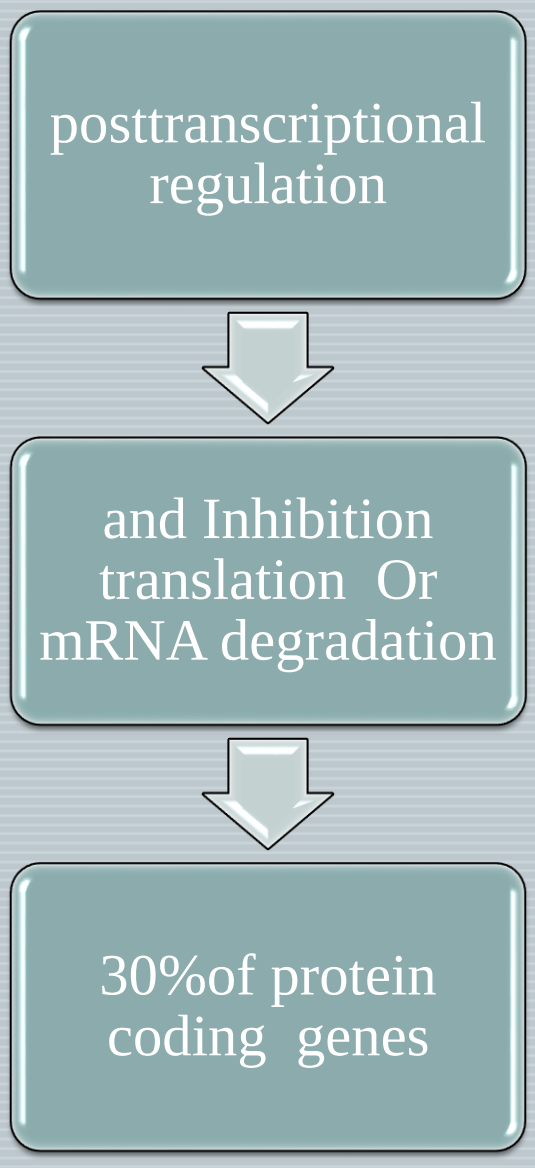


Biogenesis of miRNA

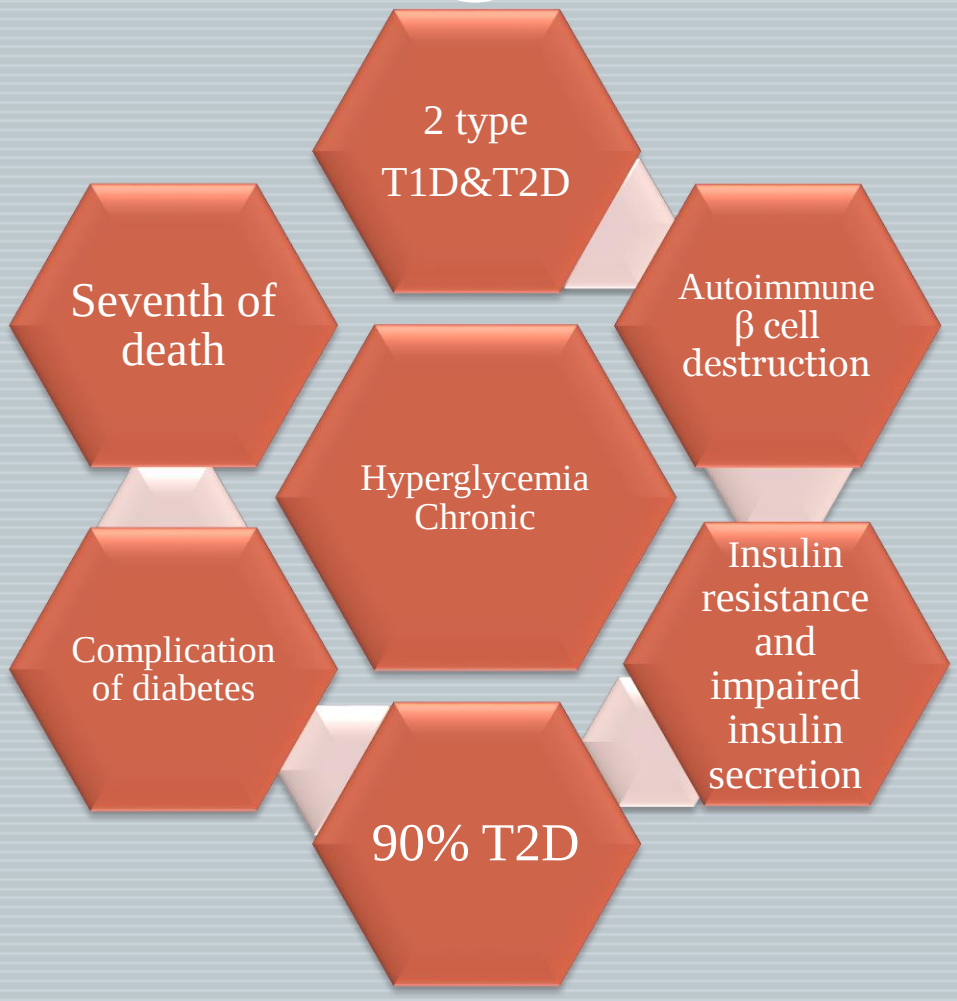


MiRNA

Function:



Diabetes


2 type
T1D&T2D
Autoimmune β cell destruction
Insulin resistance and impaired insulin secretion
90% T2D
Complication of diabetes
Seventh of death
Hyperglycemia Chronic

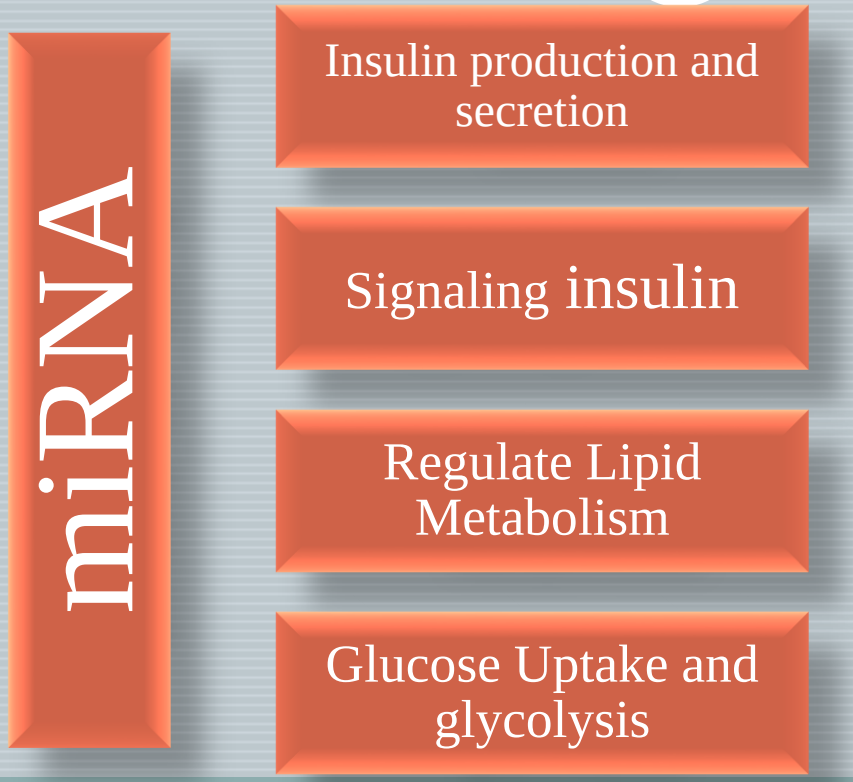
Diabetes and miRNA

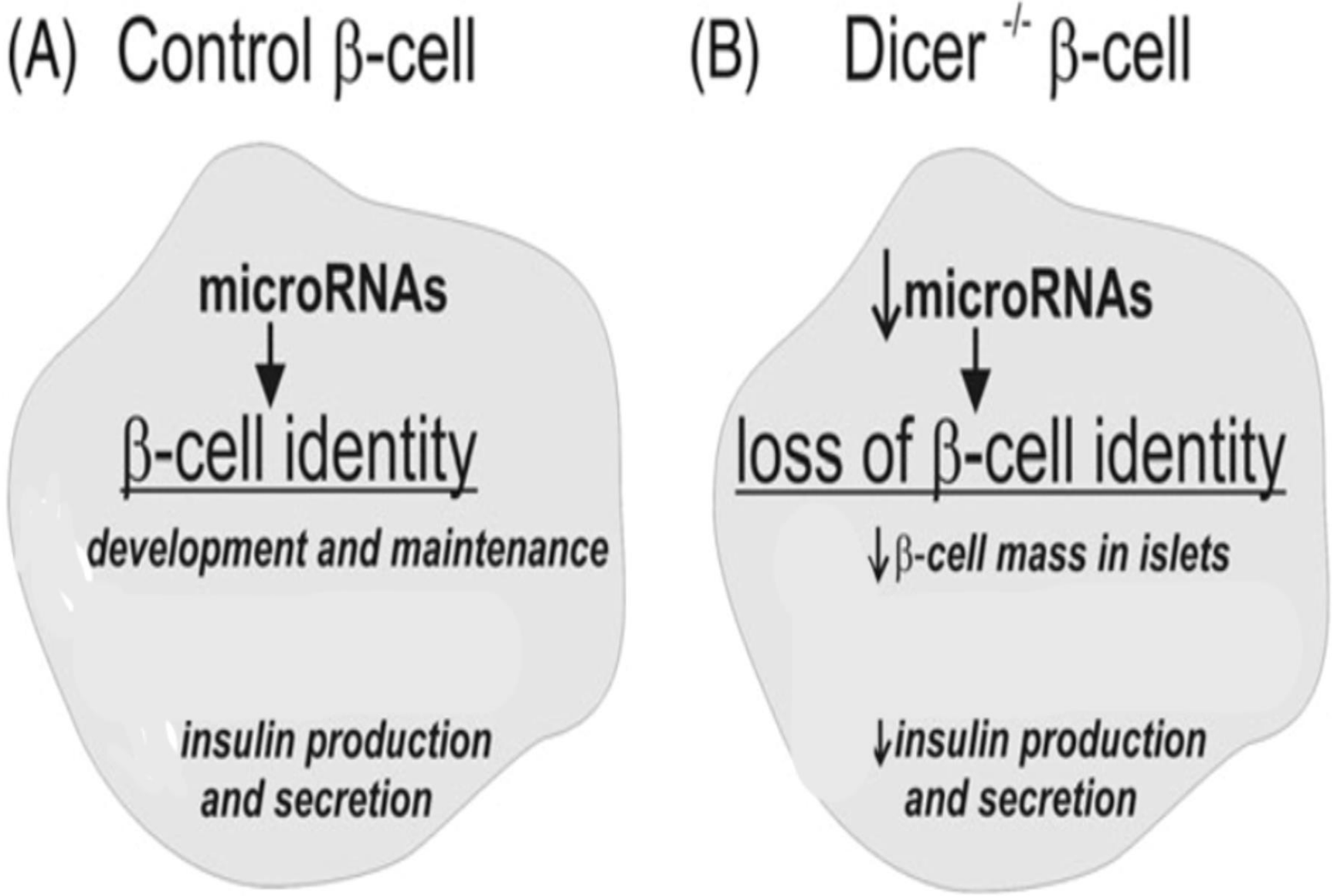
miR expression in α and β cell

roles of miRNAs in metabolism regulation, adipocyte differentiation, pancreatic development,

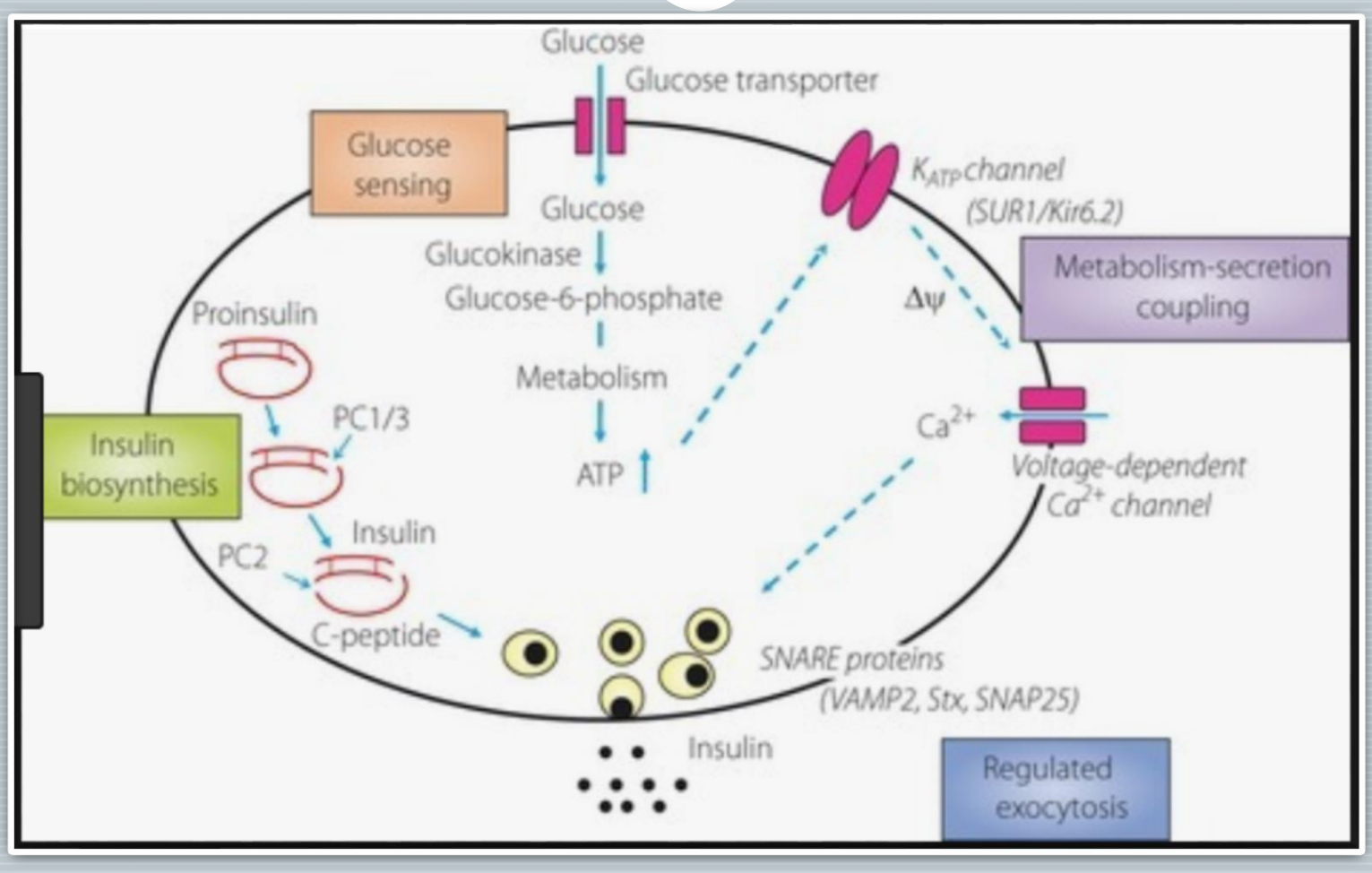
miR active role in regulating glucose homeostasis

MIRNAS IN GLUCOSE HOMEOSTASIS

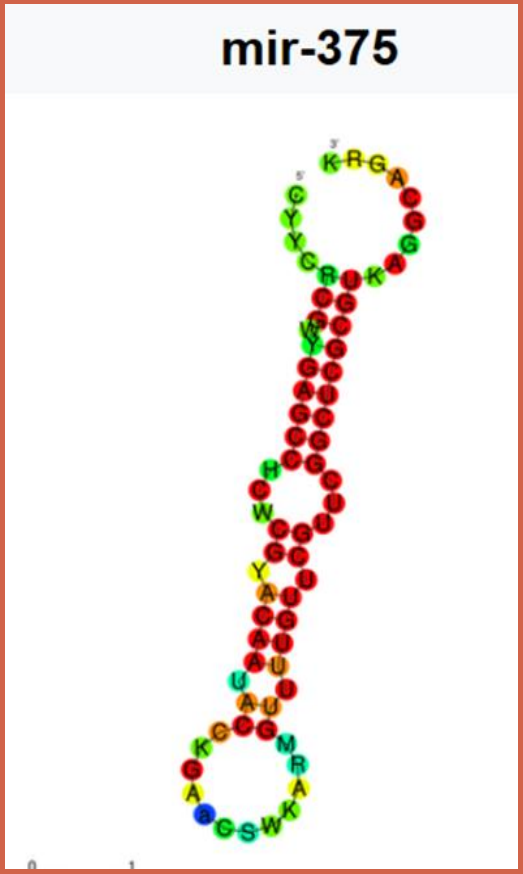


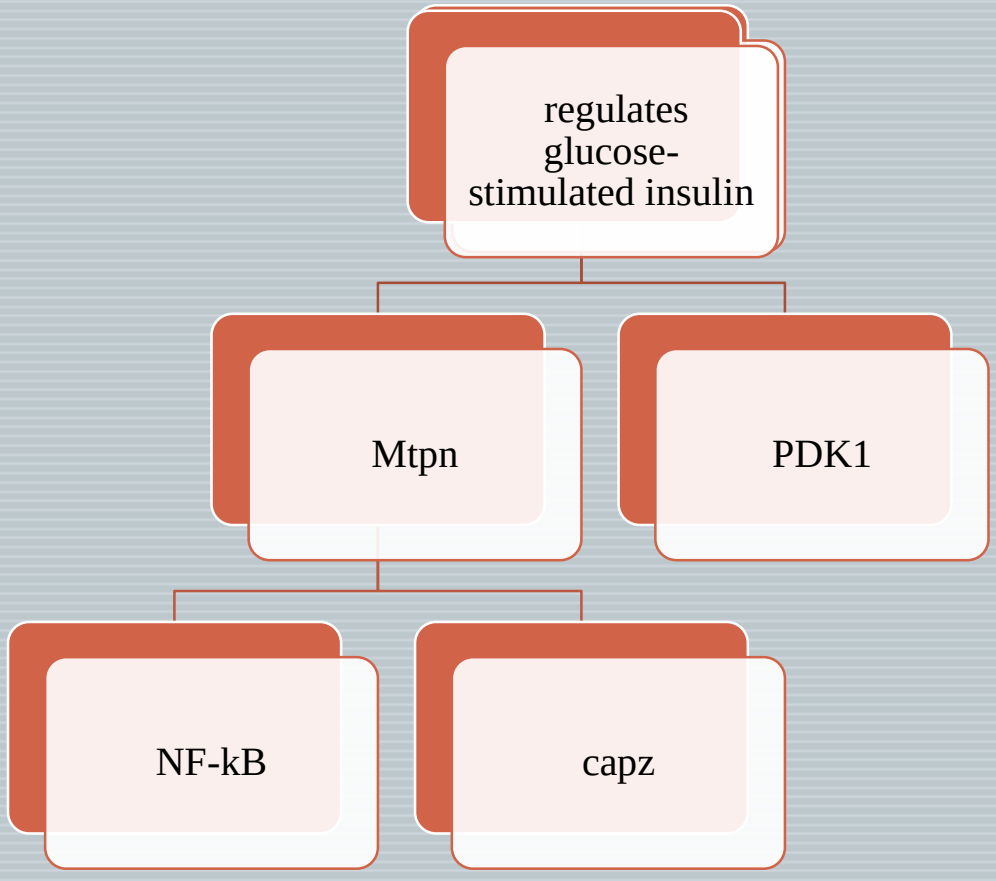

(A) Control β-cell
microRNAs
β-cell identity
development and maintenance
insulin production
and secretion
(B) Dicer -/- β-cell
↓microRNAs
loss of β-cell identity
↓β-cell mass in islets
↓insulin production
and secretion

Exocytosis Insulin

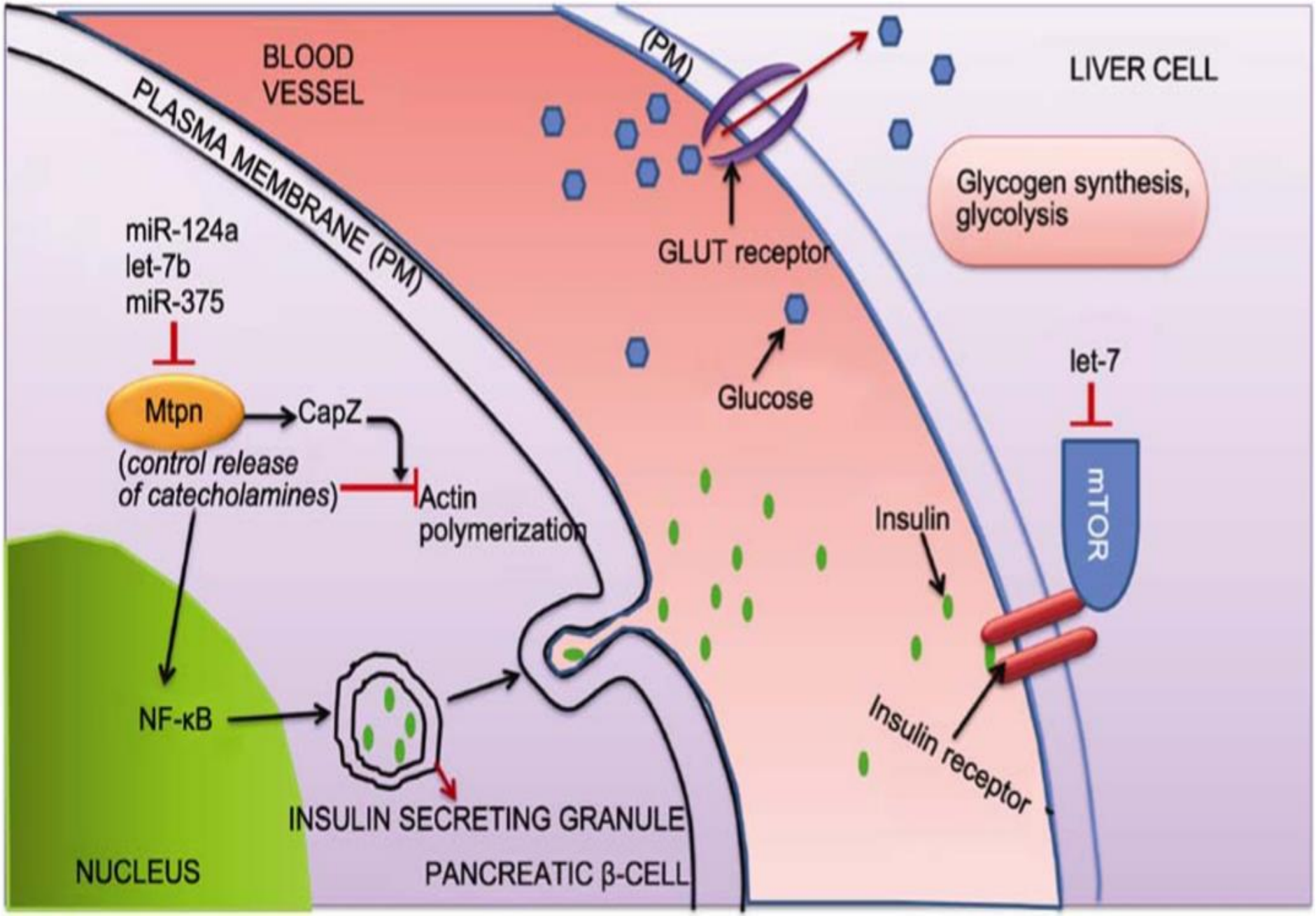


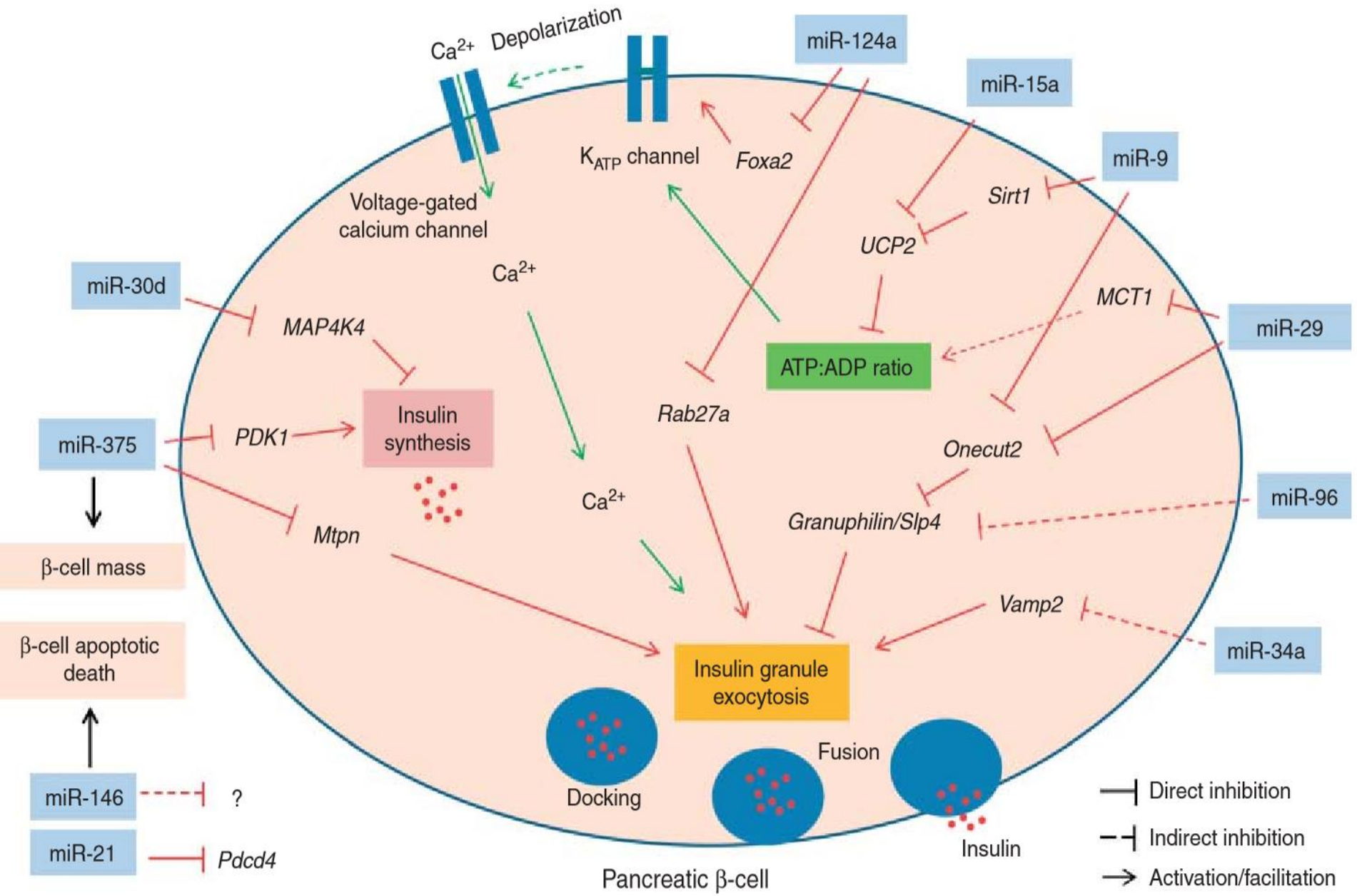
MiRNAs in insulin production and secretion



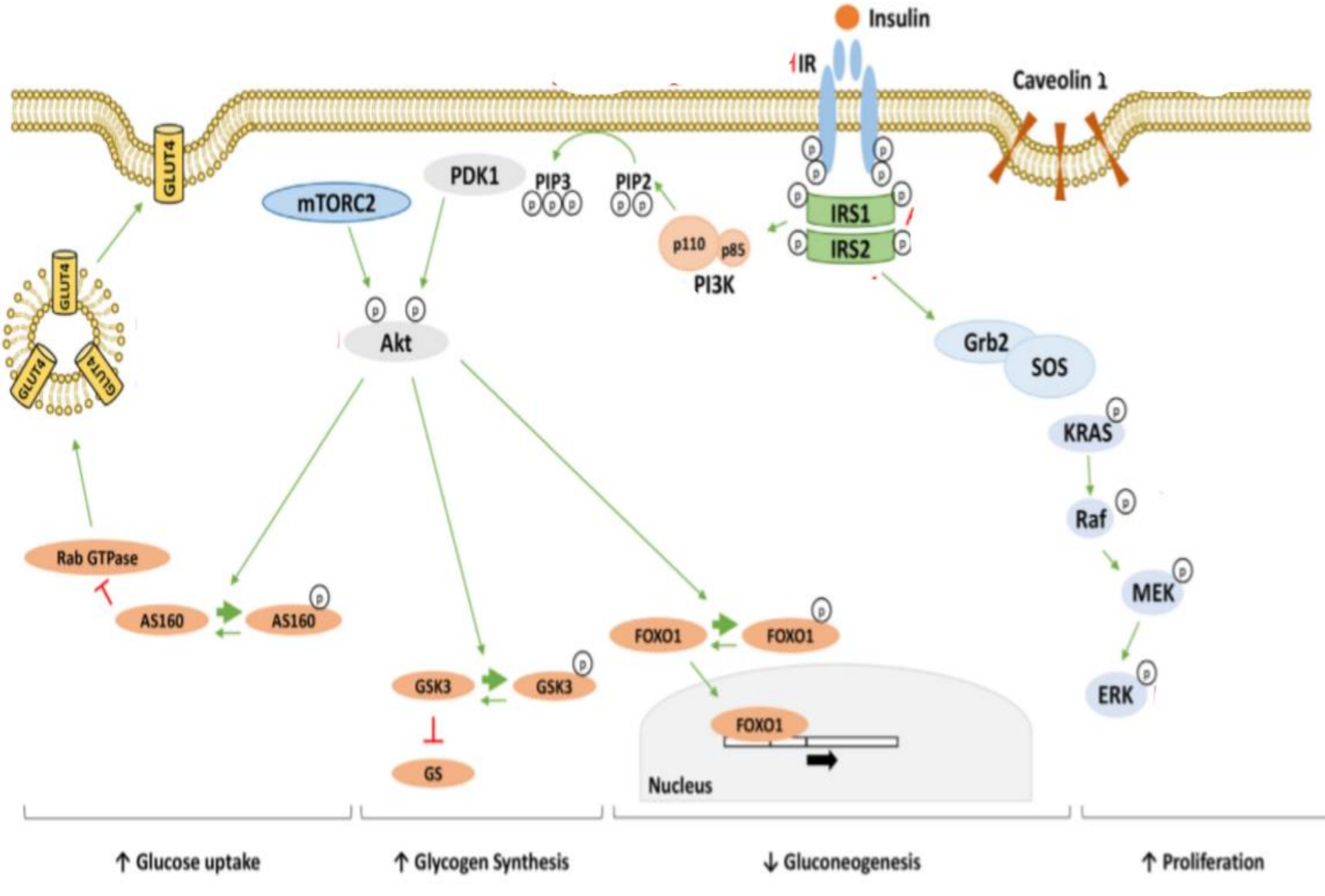


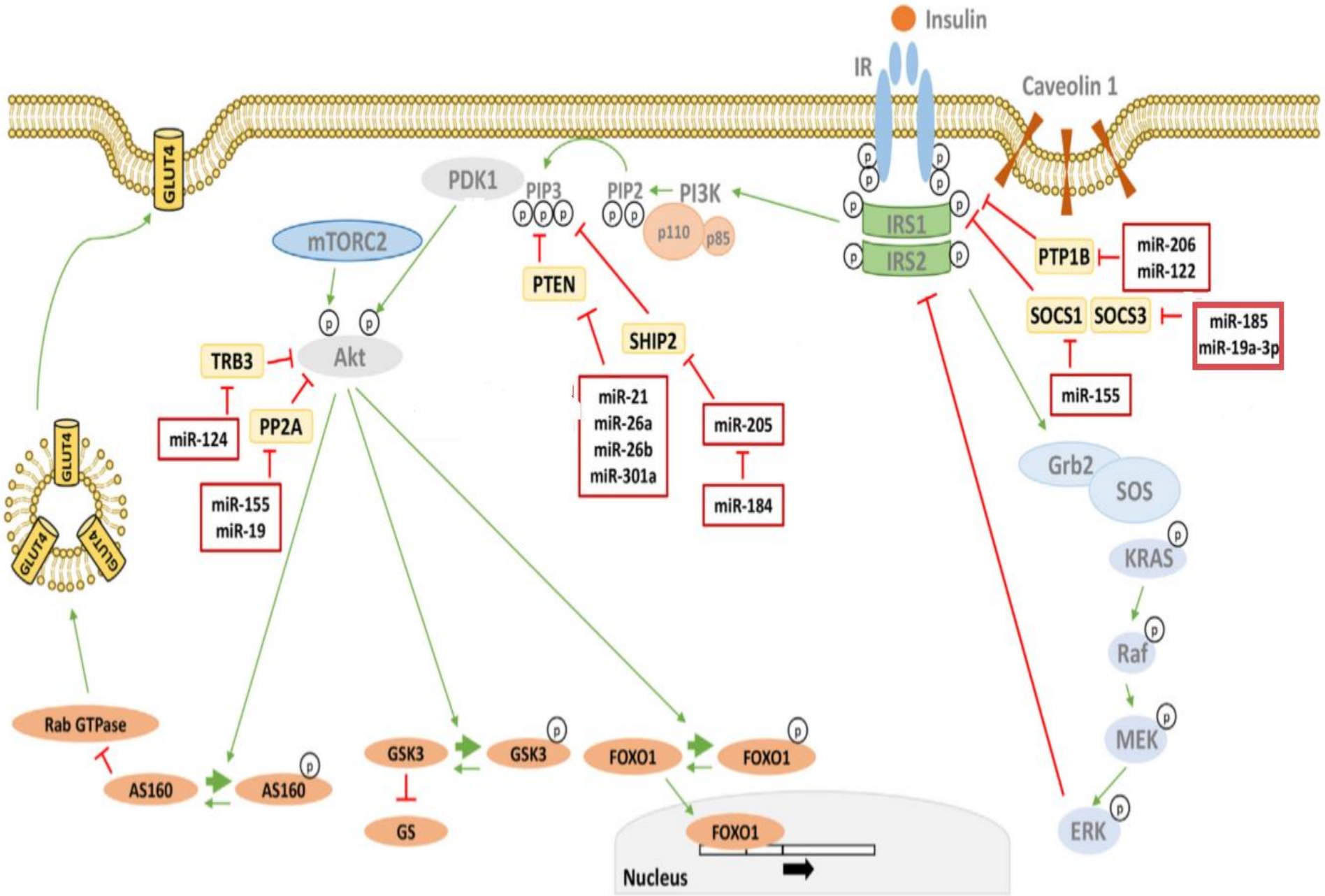
Mice with a homozygous deletion of miR-375 appear to have hyperglycemia due to decreased total pancreatic β-cell mass and insulin levels


BLOOD
VESSEL
PLASMA MEMBRANE (PM)
(PM)
LIVER CELL
Glycogen synthesis,
glycolysis
GLUT receptor
Glucose
miR-124a
let-7b
miR-375
Mtpn
CapZ
(control release
of catecholamines)
Actin
polymerization
let-7
mTOR
Insulin
NF-κB
Insulin receptor
INSULIN SECRETING GRANULE
NUCLEUS
PANCREATIC β-CELL


Ca2+ Depolarization
miR-124a
miR-15a
miR-9
KATP channel
Foxa2
Sirt1
Voltage-gated calcium channel
UCP2
Ca2+
miR-30d
MCT1
miR-29
MAP4K4
ATP:ADP ratio
Insulin synthesis
Rab27a
miR-375
PDK1
Onecut2
miR-96
Ca2+
Granuphilin/Slp4
Mtpn
β-cell mass
Vamp2
β-cell apoptotic death
miR-34a
Insulin granule exocytosis
Fusion
Docking
miR-146
?
miR-21
Pdcd4
Insulin
Direct inhibition
Indirect inhibition
Activation/facilitation
Pancreatic β-cell

Signaling Insulin

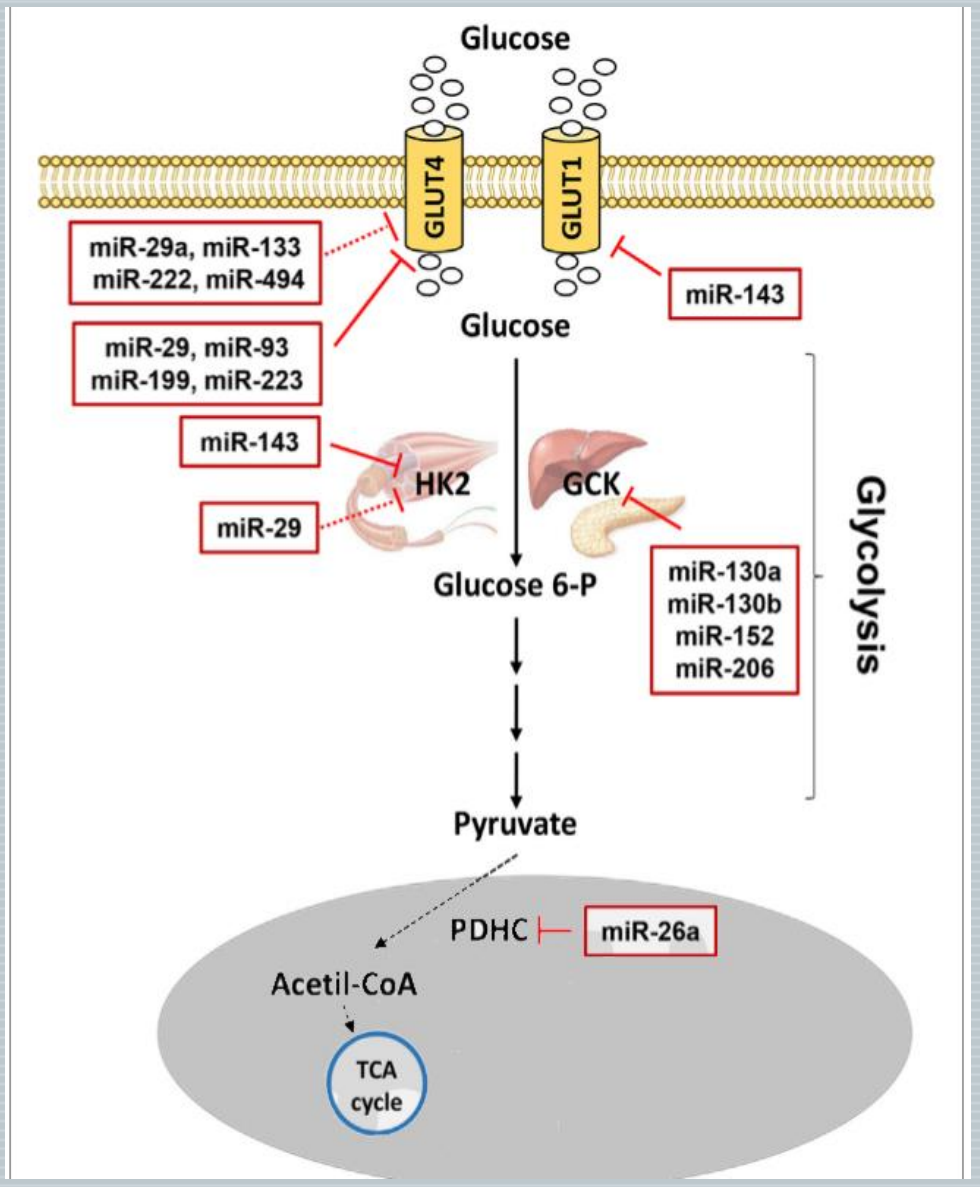



Insulin
IR
Caveolin 1
GLUT4
PDK1
PIP3
PIP2
PI3K
p110
p85
IRS1
IRS2
mTORC2
PTEN
SHIP2
PTP1B
miR-206
miR-122
SOCS1
SOCS3
miR-185
miR-19a-3p
miR-155
TRB3
Akt
miR-124
PP2A
miR-155
miR-19
miR-21
miR-26a
miR-26b
miR-301a
miR-205
miR-184
Grb2
SOS
KRAS
Raf
MEK
ERK
GLUT4
GLUT4
GLUT4
Rab GTPase
AS160
AS160
GSK3
GSK3
GS
FOXO1
FOXO1
FOXO1
Nucleus

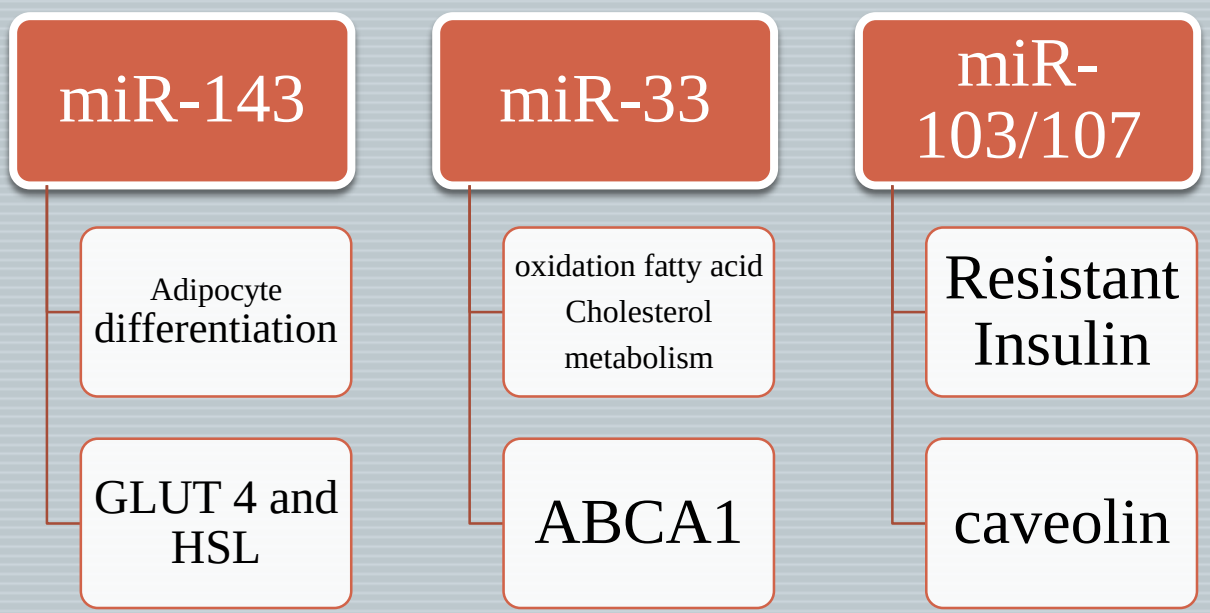
MiRNAs in insulin signaling

Target	miRNA	Cell type/tissue	Re
Insulin receptor	miR-15b	Hepatocytes	
	miR-195	HepG2	
	miR-128a	Skeletal muscle, breast	(4
	miR-144	Blood	
	miR-135	C2C12	
	Let-7	C2C12	
	miR-96	Hepatocytes	
Caveolin-1	miR-103/107	SGC7901, liver, adipose tissue	(4
	miR-124	N2A/APP695swe	
Insulin receptor substrate 1 (IRS-1)	miR-128a	Skeletal Muscle	
	miR-144	Blood	
	Let-7, lin-28	C2C12	
	miR-126	Endothelial cells	
	miR-23a	NSCLC	
	miR-29	Myocytes, Skeletal muscle	(5
	miR-145	HepG2	(5
	miR-96	Hepatocytes	
IRS-2	miR-135a	Skeletal muscle	
	miR-126	β-cells	
	miR-33a/b	Hepatocytes	
PDK1	miR-375	β-cells	
	miR-210	Endothelial cells	
Phosphatidylinositol 3-kinase	miR-128a	Skeletal muscle	
	Let-7	HepG2	
	miR-126	Endothelial cells	
	miR-503	NSCLC	
	miR-29	Skeletal muscle	
	miR-320	Adipocytes	
	miR-378	Hepatocytes	
AKT	miR-128a/b	Skeletal muscle	
	miR-145	HepG2	
	miR-126	β-cells	
	miR-143	Liver	
	miR-1	H9C2	
	miR-423	Hepatocytes	
	miR-29	Adipocytes	

MiRNA in Glucose Uptake and glycolysis and Oxidative metabolism



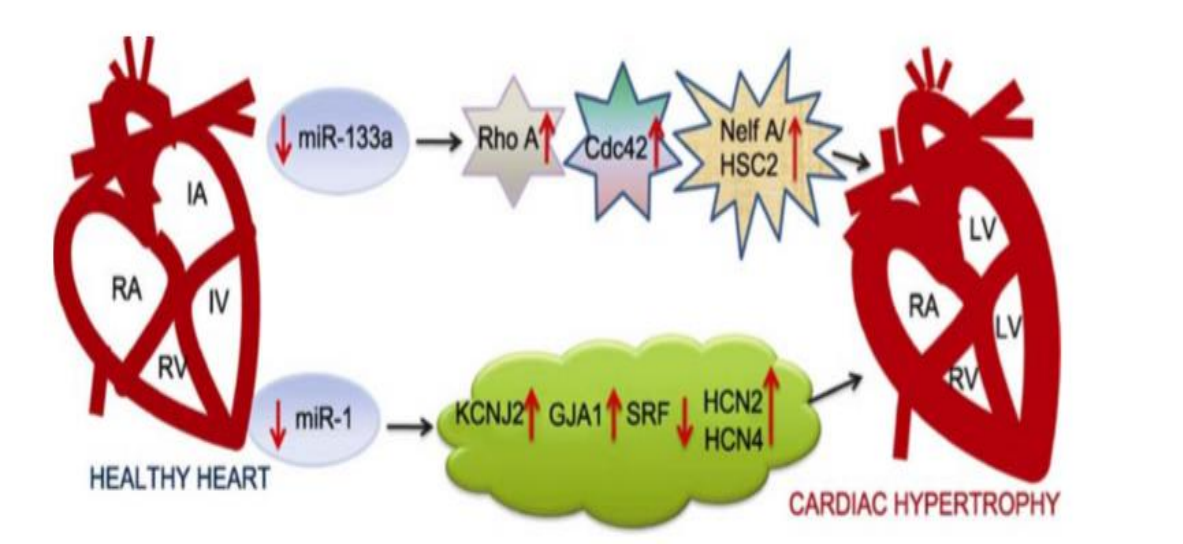
MiRNAs Regulate Lipid Metabolism and Insulin Action in Adipose Tissue



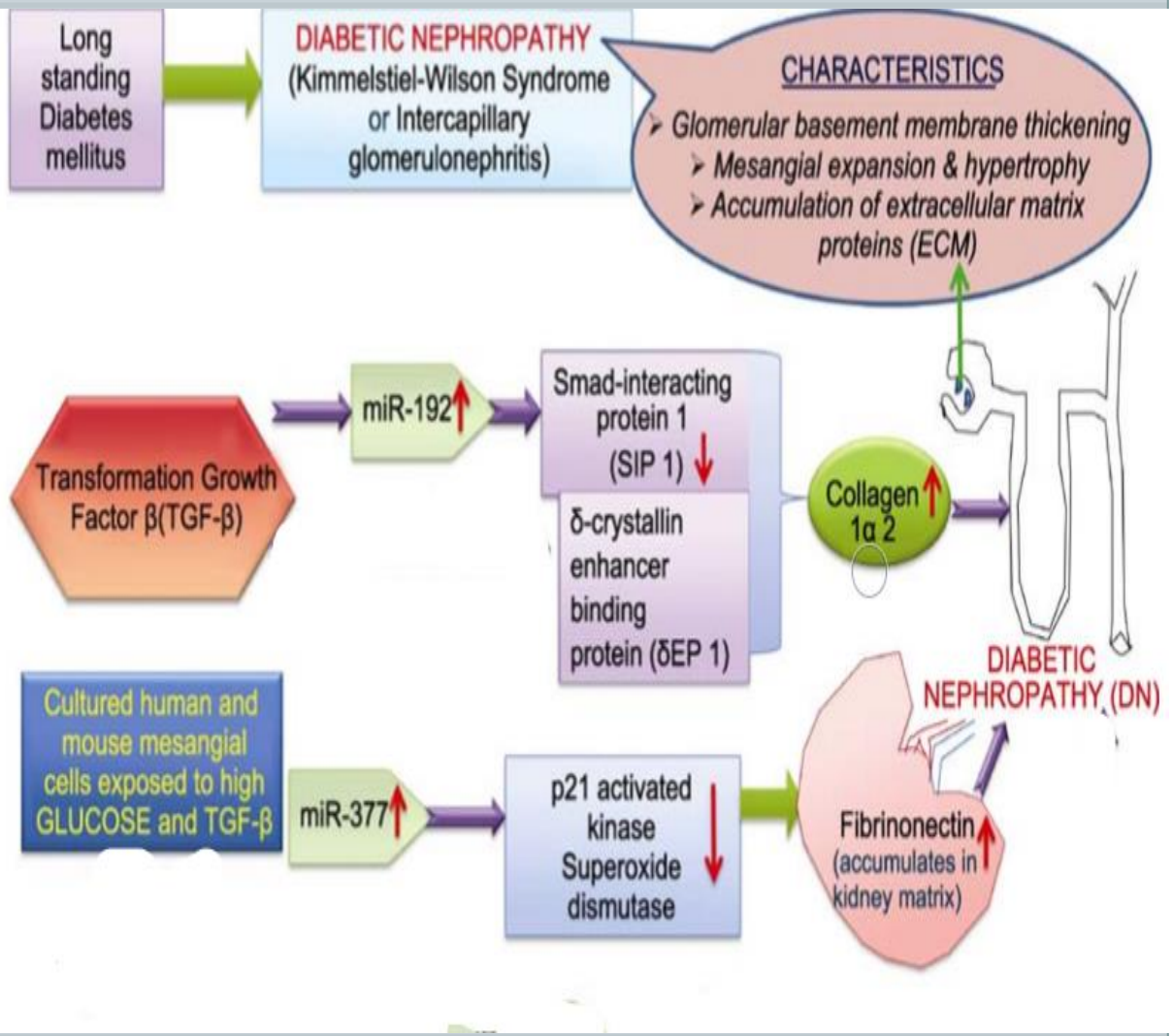
MIRNAS IN DIABETIC COMPLICATIONS

Diabetes causes complications in many organs, such as heart, kidney, eye, and foot, and miRNAs are involved in many of these complications

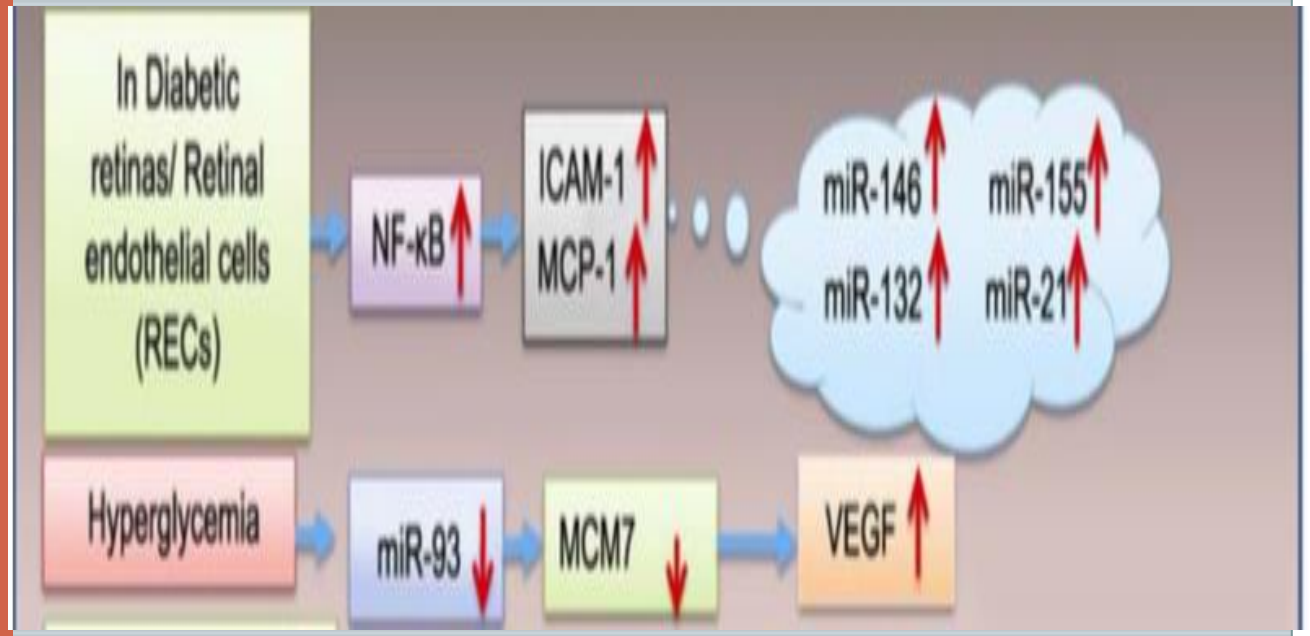
Diabetic cardiomyopathy



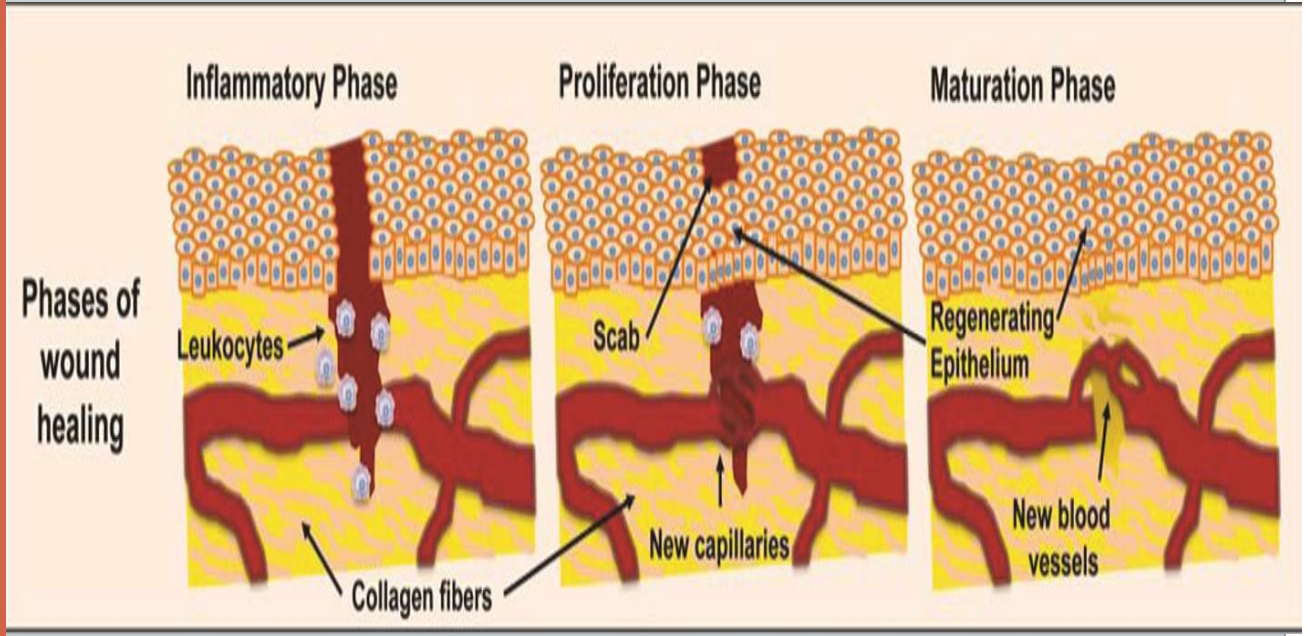
Diabetic nephropathy



Diabetic retinopathy

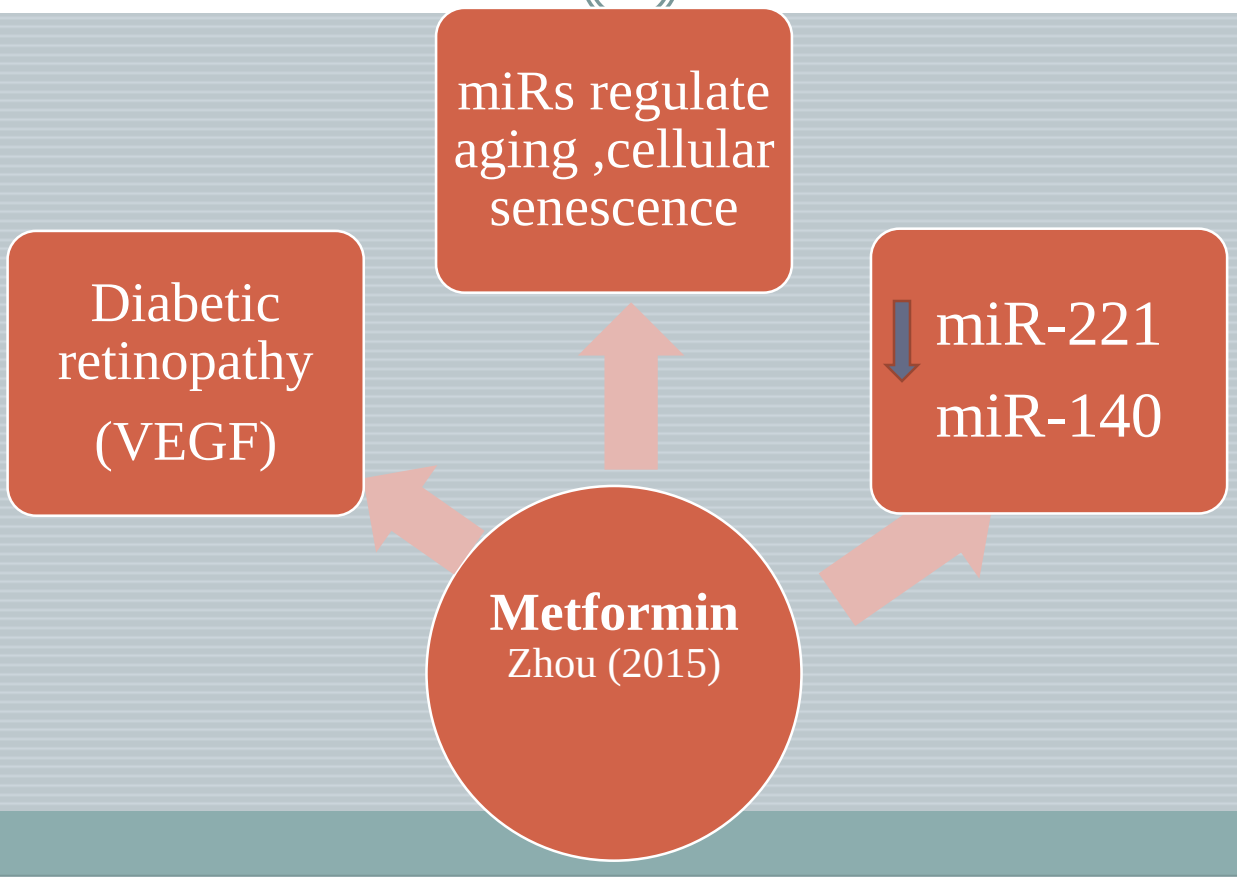


Ulcer foot diabetic

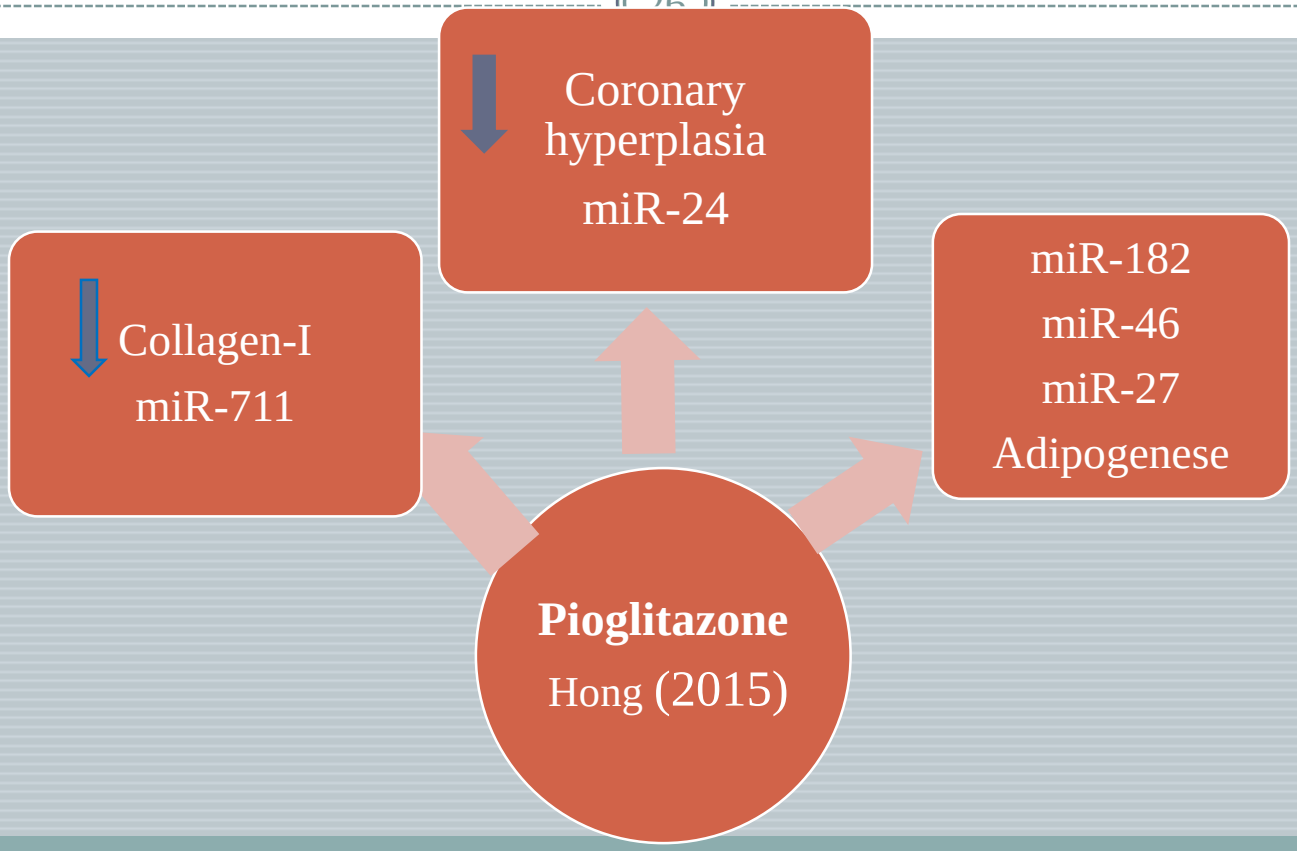


Inflammatory Phase	Proliferation Phase	Maturation Phase
miR-16 miR-126 miR-203	miR-21 miR-126 miR-328	miR-29 miR-196

Effects of antidiabetic drugs on miRs



Effects of antidiabetic drugs on miRs



Effects of antidiabetic drugs on miRs

Linaglipin

Kanasaki(2014)

↑ miR-29

Improve nephropathy

Exenatide

Lee IS(2016)

miR-29
miR-124
miR-375

Ameliorate insulin sensitivity

Liraglutide

Li J(2017)

↓ Apoptosis beta cell

miR-375
miR-139

conclusion

MicroRNA are detectable and stable in body fluids and that altered circulating miRNA profiles are associated with metabolic diseases, including T2D .

MiRNAs as biomarkers drug targets in prevention, treatment And management of diabetes and its complication.


Thank you for your attention