Table SI. Specific molecular mechanisms of miR-146a regulating cardiovascular diseases.

Disease	Mechanism	Impact	(Refs.)
Sepsis-induced cardiomyopathy	miR-146a↑→IRAK1,TRAF6↓→NK-κB↓→TNF-α, IL-1β,IL-6,ICAM-1,VCAM-1↓→Inflammation↓;	Alleviate	(83)
	miR-146a↓→DLST↓→Energy metabolism disorder↑;	Aggravate	(84)
Myocardial ischemia-reperfusion injury	miR-146a↑→NF2↓→Rac1/PAK1↑→VEGF angiogenic ability↑; miR-146a↑→Nox4↓→SOD↑,MDA↓→ROS↓; lncRNA SOX2-OT↓→miR-146a-5p↑→→TNF-α,IL-1β,IL-6, MDA↓,SOD↑→Inflammation and ROS↓;	Alleviate	(85,86,88)
	circRNA Fbxl5→miR-146a↓→MED1↑→Cardiomyocyte apoptosis↑; miR-146a↓→MED1/TRAP220↑→Bax/Bcl-2 ratio,caspase-3↑→Cardiomyocyte apoptosis↑;	Aggravate	(41,87)
Myocardial infarction	miR-146a↑→TRAF6↓→p-p38↓→caspase-3↓→Apoptosis↓; miR-146a↓→AKT/ERK↓→ANP,BNP,ST2,NE,COL-I,COL-III↓→Heart failure↓; miR-146a↑→TRAF6↓→Inflammation↓;	Alleviate	(89,91,94)
	miR-146a↑→M1 polarization↑, M2 polarization↓→Inflammation↑;	Aggravate	(94)
Myocardial fibrosis	miR-146a↑→IRAK1,TRAF6↓→NK-κB↓→α-SMA↓→Fibrosis↓; miR-146a-5p↑→FGF2↓→α-SMA,COL-1↓→Fibrosis↓; miR-146a-5p↑→TXNIP↓→NK-κB↓→E-cadherin↑,α-SMA↓→EndMT↓→Fibrosis↓;	Alleviate	(55,96,97)
Atherosclerosis	miR-146a-3p↓→HDAC1,IKBα→KLF5↓→Inflammation and apoptosis↓→Plaque stability↑; miR-146a↓→p53,cyclinD1↑→vascular smooth muscle proliferation↑;	Alleviate	(98,100)

ERK,mitogen-activated protein kinase;ANP, atrial natriuretic peptide;BNP, brain natriuretic peptide;COL-1, collagen type 1; DLST, dihydrolipoamide S-succinyltransferase;E-cadherin, epithelial cadherin;EndMT, endothelial-mesenchymal transition;Fbxl5, F-box and leucine-rich repeat protein 5;FGF2, fibroblast growth factor 2;HDAC1, histone deacetylase 1;ICAM-1, intercellular adhesion molecule 1;IRAK1, interleukin-1 receptor-associated kinase 1;KLF5,Krüppel-like factor 5;lncRNA, long non-coding RNA;MDA, malondialdehyde;MED1, mediator complex subunit 1;NF2, neurofibromin 2;NE, norepinephrine;Rac1, Ras-related C3 botulinum toxin substrate 1;PAK1, p21-activated kinase 1;ROS, reactive oxygen species; α-SMA,α-smooth muscle actin; SOD, superoxide dismutase;SOX2-OT, SOX2 overlapping transcript;ST2, suppression of tumorigenicity 2;TRAF6, TNF receptor-associated factor 6; TRAP220, thyroid hormone receptor-associated protein 220;TXNIP,thioredoxin-interacting protein;VCAM-1, vascular cell adhesion molecule 1; VEGF, vascular endothelial growth factor.

Table SII. Specific molecular mechanisms of miR-146a regulating endocrine metabolic disorders.

Disease	Mechanism	Impact	(Refs.)
Vascular diseases	miR-146a↑→IRAK1,TRAF6↓→NK-κB↓→Inflammation↓; Troxerutin→miR-146a↑→IRAK1,TRAF6↓→NK-κB↓→TNF-α, IL-1β,IL-6,ICAM-1↓→Inflammation↓;	Alleviate	(43,44,118)
Diabetic peripheral neuropathy	miR-146a↑→IRAK1,TRAF6↓→NK-κB↓→M2 polarization↑, TNF-α, IL-1β↓→Inflammation↓;	Alleviate	(121)
Diabetic nephropathy	miR-146a↑→ErbB4-Notch1↓→Podocyte damage↓; miR-146a↑→ErbB4-EGFR↓,TGF-β1/Smad3→↓→Podocyte damage↓; miR-146a↑→Nox4↓→SOD↑,MDA↓,VCAM-1,ICAM-1↓→ROS and inflammation↓; 6-gingerol→miR-146a↑→TLR4/TRAF6/NLRP3↓→Inflammation↓; miR-146a-5p↑→TRAF6↓→STAT1↓→M2 polarization↑→Inflammation↓;	Alleviate	(37, 62,125-127)
Diabetic foot ulcers	miR-146a↑→TLR4↓→NK-κB↓→M2 polarization↑, TNF-α, IL-6,iNOS↓→Inflammation↓;	Alleviate	(131)
	miR-146a↓→GRP78, CHOP, ATF-6, IRE-1, PERK↑, P22PHOX, TRPC-6, TXNIP↑→ERS and ROS↑;	Aggravate	(132)

ATF-6,activating transcription factor 6;CHOP,C/EBP homologous protein;EGFR,epidermal growth factor receptor;ERS,endoplasmic reticulum stress;ErbB4,erythroblastic leukemia viral oncogene homolog 4;GRP78,glucose-regulated protein 78;iNOS,inducible nitric oxide synthase;IRAK1,interleukin-1 receptor-associated kinase 1;IRE-1,inositol-requiring enzyme 1;ICAM-1,intercellular adhesion molecule 1;MDA,malondialdehyde;PERK,protein kinase RNA-like endoplasmic reticulum kinase;P22PHOX,phagocyte oxidase 22;ROS, reactive oxygen species; SOD,superoxide dismutase;STAT1,signal transducer and activator of transcription 1;TLR4,toll-like receptor 4;TRAF6,TNF receptor-associated factor 6;VCAM-1,vascular cell adhesion molecule 1.