Supplementary Information

Table S1. Possible PDT-related mechanisms and association with targets predicted for "resistive-" and "phototox-miRs".

Mechanism	MiR(s)	Target(s)/GO Terms	p/v	Enriched Targets in the Corresponding GO Terms	Function	(Citation)
response to oxidative stress	130a	"response to oxidative stress"		GO: 0006979, SLC11A2, APOA4, FOS, HIF1A, G6PD, SIRT7, PRDX3	tox	-
cellular glutathione content	130a	negative correlation with GSH levels	-	-	tox	[104]
thioredoxin redox system	130a	PRDX3	p	-	tox	[9,51]
NF-κB	25, 130a, *203*, *20a**	"positive regulation of NF-κB transcription factor activity"	-	GO: 0051092, miR-25: IL6, TNF, KRAS, IL1B, TLR4, TGFB1, miR-130a: IRAK1, RELA, IL1B, PRDX3, IKBKB, TGFB1, miR-203: IL6, TNF, KRAS, IL1B, TLR4, IKBKB, TGFB1, miR-20a*: IL6, TNF, KRAS, RIPK1, NPM1, TGFBR3, IL1B, MALT1, TGFB1	tox	[62,105]
	25	TRAF6	p	-	inv	
	106b	MAP3K8	p	-	tox	
AP-1	326	HDAC10	p	-	res	[106,107]
	330-5p	HDAC3	p	-	res	
Nrf2	141, 200a, 130a, 93*	KEAP1	p	-	res	[9,29,74,82]
		NFE2	v		tox	
	326	NFE2	p		tox	
HIF-1α	*141*, *200c*, *135a*, *20a**	HIF-1α	v	-	tox	[52,53,55,108]
	130a	HIF-1α	p	-	tox	
	106b, 939	ARNT2	p	-	tox	
	106b, 93*, *141*, *200a*, *20a** *200b*, *200c*, *330*	VEGFA	v	-	tox	
	130a	"positive regulation of angiogenesis"	-	GO: 0045766, CHIF1A, F3, IL1B, NOS3, IL1A	tox	

Table S1. *Cont.*

Mechanism	MiR(s)	Target(s)/GO Terms	p/v	Enriched Targets in the Corresponding GO Terms	Function	Function (Citation)
JNK and p38 pathway	200a, 200b, 200c, 429, 203, 20a*	"positive regulation of MAP kinase activity"	-	GO: 0043406, miR-200c: EGFR, PROK2, KRAS, ERBB2, MET, MAP3K10, ZEB2, HGF, PAK1, EGF, TGFB1, miR-200a: EGFR, KRAS, PDGFB, MET, MAP3K10, ZEB2, HGF, EGF, THBS1, TGFB1, HTR2A, miR-200b: EGFR, PROK2, MET, MAP3K10, ZEB2, EGF, THBS1, TGFB1, miR-429: EGFR, PDGFB, CXCR4, MET, MAP3K10, ZEB2, EGF, TGFB1, miR-203: TNF, KRAS, IL1B, ZEB2, HGF, KIT, ADRA2B, TGFB1, SYK, miR-20a*: EGFR, ERCC6, TNF, KRAS, RIPK1, MET, IL1B, THBS1, TGFB1	res	[9,47,49]
	203	"positive regulation of MAPKKK cascade"	-	GO: 0090080, HIF1A, F3, IL1B, NOS3, IL1A	res	
	200c, 203	"regulation of JNK cascade"	-	GO: 0007254, miR-200c: AKT1, MAP3K10, ZEB2, PAK1, PDCD4, TP73, miR-203: AKT1, TNF, IL1B, ZEB2, TLR4, SYK	inv	
	203, 200c	"regulation of stress-activated protein kinase signaling pathway"	-	GO: 007030, miR-203: TNF, IL1B, TLR4, TGFB2, miR-200c: AKT1, MAP3K10, ZEB2, PAK1, PDCD4, TP73, TGFB2	inv	
	25	TRAF6	p	-	inv	
	106b	TRAF4	p	-	inv	[109]
	106b	MAP3K8	p	-	inv	[105]
PI3K/Akt	130a	"regulation of protein kinase B signaling cascade"	-	GO: 0051896, F3, TSC2, PTEN, TGFB1	inv	[30,64,65]
	130a	"protein kinase B signaling cascade"		GO: 0043491, AKT1, TSC2, PIK3CA, RPS6KB1	tox	
	106b, 130a, 93*, *20a**	AKT1	v	-	tox	
	25	AKT2	v	-	tox	
Ras signaling	326	"Ras protein signal transduction"	-	GO: 0007265, RHOJ, MAPKAPK2, ARHGEF11, NRAS, PLCE1, KRAS, CDC42EP1, SOS1, PTH, COL1A2, RHOA, CDC42EP4, RHOG, CDC42EP5	res	[49]
	25	SESN3	p	-	tox	
	130a, 93*	SESN2	p	-	tox	

Table S1. *Cont.*

Mechanism	MiR(s)	Target(s)/GO Terms	p/v	Enriched Targets in the Corresponding GO Terms	Function	Function (Citation)
HSP modulation	106b	HSPA6, HSPA8	p	-	tox	[9,85–87]
	489	HSPA9	p	-	tox	
	664	HSPA1B	p	-	tox	
	326	HSPA2, HSPA6, HSPB7, HSP27, HSPB8	p	-	tox	
	141, *200a*	HSPA4L	p	-	tox	
	203	HSPA14	p	-	tox	
(Mitochondrial) apoptosis promotion	25, *200c*, *200b*, *20a**	BCL2	v		tox	[66,68,80]
	200c, 203	BAX	v		res	
	200c, 20a*, *106b*	"activation of pro-apoptotic gene products"	-	GO: 0008633, miR-106b: AKT1, BCL2, PPP3R1, MYC, BCL2L11, miR-200c: AKT1, BCL2, FAS, MYC, miR-20a*: AKT1, RIPK1, BCL2, MYC, BCL2L11	res	
	106b, 200c, 203, 200b, 20a*	"release of cytochrome c from mitochondria" "apoptotic mitochondrial changes"	-	GO: 0001836, miR-106b: BBC3, JUN, BCL2, TP53, MYC, TP73, miR-200c: BCL2, BAX, TP53, MYC, TP73, miR-200b: JUN, BCL2, TP53, MYC, miR-203: CASP3, JUN, BAX, TP53 GO: 0008637, miR-106b: AKT1, BBC3, JUN, BCL2, TP53, MYC, TP73, miR-200c: AKT1, BCL2, BAX, TP53, MYC, TP73, miR-200a: AKT1, SH3GLB1, JUN, TP53, MYC, miR-200b: AKT1, JUN, BCL2, TP53, MYC, miR-203: AKT1, CASP3, CDKN2A, JUN, BAX, TP53, miR-20a*: AKT1, CDKN2A, JUN, BCL2, TP53, MYC	res	
	664, 203	CASP3	p	-	res	
	590-5p	CASP8	p	-	res	
	203	DIABLO	p	-	res	
NO synthase inhibition	200c, 20a*	"regulation of nitric-oxide synthase activity"	-	GO: 0050999, miR-200c: EGFR, AKT1, HIF1A, KRAS, miR-20a*: EGFR, AKT1, HIF1A, KRAS	inv	[83,84]
	203, *20a**	"positive regulation of nitric oxide biosynthetic process"	-	GO: 0045429, miR-203: AKT1, TNF, IFNG, IL1B, miR-20a*: EGFR, AKT1, TNF, IFNG, KLRK1, IL1B, JAK2	tox	
	203, *20a**	NOS2A	v	-	tox	
	939, *135a*, *135b*	NOS2A	p	-	tox	
	130a	NOS3	v	-	tox	

Table S1. *Cont.*

Mechanism	MiR(s)	Target(s)/GO Terms	p/v	Enriched Targets in the Corresponding GO Terms	Function (Citation)	
NADPH oxidases	25	NOX4	v	-	tox	[47,69–71,78]
	93*	NOX4	p			
	200a, 141	NOX1	p	-	res	
Sirtuin proteins	130a	SIRT7, SIRT6	p	-	tox	[47,56]
	200a, 200b, 200c, 429 and 135a, *93**	SIRT1	v	-	res	
Disruption of heme degradation pathway	*20a**	HMOX1	p	-	tox	[73,75–77]
	25	HMOX2	p			
	141, 200a	BACH1	p	-	res	
G1/S cycle inhibition	25, *106b*	"G1 phase of mitotic cell cycle"	-	GO:0000080, miR-25: E2F1, CDKN1C, CDC6, CDK6, CDK2, miR-106b: E2F1, CDKN1C, CDC23, CDK2	tox	[72]
	200a, *200b*, *200c*	"G1/S transition of mitotic cell cycle"	-	GO:0000082, miR-200c: EGFR, AKT1, CDKN1A, CCND1, CDKN1B, CCND2, BCL2, miR-200a: EGFR, AKT1, CCND1, CDKN1B, CCND2, CDKN3, miR-200b: EGFR, AKT1, CCND1, CDKN1B, CCND2, BCL2, SKP2	tox	
Modulating arachidonic acid cascade	*141*, *200c*, *200a*	LOX	v	-	tox	[88]
	664	LOX	p	-	tox	
Microsomal glutathione *S*-transferase 1	93*	MGST1	-v	-	tox	[29]

Explanations: *potentially conflicting results*; tox: associated with PDT phototoxicity; res: associated with PDT insensitivity; inv: involvement; p: predicted target; v: validated target.