

Circulating miRNAs, Insulin Sensitivity,
and Associated Metabolic Risk Factors
(e.g., dyslipidemia and elevated blood pressure)
in Humans

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Patient Characteristics

Age (yrs)	39.0 ± 10.3
Sex	55 female, 26 male
Race	1 Asian, 42 Black, 37 White, 1 Hispanic
Body Mass Index (kg/m ²)	31.4 ± 5.2
Waist Circumference (cm)	97.4 ± 14.1
Systolic Blood Pressure (mmHg)	116.8 ± 14.1
Diastolic Blood Pressure (mmHg)	68.1 ± 9.5
Triglycerides (mg/dL)	110.0 ± 58.6
HDL-cholesterol (mg/dL)	50.0 ± 20.5
Glucose Disposal Rate (mg/min/kg LBM)	14.4 ± 4.7
Fasting glucose (mg/dL) (n=80)	92.9 ± 10.9
Fasting insulin (μU/mL) (n=48)	19.3 ± 12.6
Total body fat (%)	41.1 ± 10.0
Total fat mass (kg) (n=71)	34.9 ± 11.7

Relationship of miRNA and Insulin Sensitivity

miR	n	R ²	p-value
miR-16	81	0.0873	0.0074**
miR-33	52	0.0526	0.1018
miR-34a	44	0.0005	0.8851
miR-107	56	0.0746	0.0417*
miR-133a	73	0.0177	0.2623
miR-140	66	0.0163	0.3072
miR-150	81	0.0334	0.1025
miR-199a	67	0.0436	0.0898
miR-222	81	0.0321	0.1097

Relationship of miRNA and insulin sensitivity after adjusting for BMI

miR	n	Unadjusted Model		Adjusted Model (+BMI)		
		R ²	p-value	miR Partial β	Model R ²	Model p-value
miR-16	81	0.0873	0.0074**	0.25*	0.2183	<0.0001**
miR-33	52	0.0526	0.1018	0.26*	0.1814	0.0028**
miR-34a	44	0.0005	0.8851	0.05	0.0693	0.0865
miR-107	56	0.0746	0.0417*	0.32**	0.2310	0.0004**
miR-133a	73	0.0177	0.2623	0.13	0.1496	0.0013**
miR-140	66	0.0163	0.3072	0.12	0.1559	0.0018**
miR-150	81	0.0334	0.1025	0.21*	0.1994	<0.0001**
miR-199a	67	0.0436	0.0898	0.22	0.1807	0.0006**
miR-222	81	0.0321	0.1097	0.20*	0.1962	<0.0001**

Correlation of miRs and metabolic risk factors

	r	p-value
miR-16 (n=81)		
Waist Circumference (cm)	-0.25	0.0221
Triglycerides (mg/dL)	-0.28	0.0116
HDL cholesterol (mg/dL)	0.22	0.0468
miR-33 (n=52)		
Systolic Blood Pressure (mmHg)	-0.29	0.0393

Summary

- Two of the 12 candidate miRs were positively associated with insulin sensitivity, as measured by the gold-standard clamp technique: **miR-107** and **miR-16**
 - After adjustment with BMI, an additional 3 miRs were also positively associated with insulin sensitivity: **miR-150**, **-33**, and **-222**.
- Some of these same miRs were also associated with metabolic syndrome traits
 - **miR-16**: **WC**, **triglycerides**, and **HDL**
 - **miR-33**: **systolic BP**

Implications

- These miRs have the potential to serve as biomarkers for insulin sensitivity in humans, and/or may be involved in the development of insulin resistance
- As some miRs were shown to be associated with multiple metabolic traits, these miR may additionally act as mediators for diseases characterized by insulin resistance
- However, since multiple miRs can be related to single traits, the data suggest that multiple miRs affecting different pathways may work in concert to regulate systemic metabolism.