

Supplemental Data

Table S1: Differentially expressed miRNAs acute respiratory distress vs control. Significance tested by Wilcoxon's t-test (n=21 acute respiratory distress, n=14 control).

miRNA	Fold Change	P-value
miR-181a-5p	1.88	4.11E-03
miR-16-5p	1.91	6.97E-03
miR-375	1.62	8.47E-03
miR-345-5p	1.29	8.68E-03
miR-590-5p	1.45	1.33E-02
miR-186-5p	1.28	1.40E-02
miR-374a-5p	1.82	1.60E-02
miR-125b-5p	1.57	1.80E-02
miR-26a-5p	1.80	2.46E-02
miR-126-3p	1.78	2.60E-02
miR-195-5p	1.49	3.12E-02
miR-374b-5p	1.87	3.24E-02
miR-331-3p	1.48	4.16E-02
miR-142-3p	1.75	4.41E-02
miR-139-5p	1.59	4.88E-02

Table S2: Differentially expressed miRNAs in patients with bacterial LRTI, ARDS vs control. Significance tested by Wilcoxon's t-test (n=11 ARDS, n=8 control). ARDS-Acute respiratory distress syndrome, LRTI-lower respiratory tract infection.

miRNA	Fold Change	P-value
miR-324-3p	1.47	2.54E-03
miR-186-5p	1.38	1.57E-02
miR-590-5p	1.59	1.86E-02
miR-200c-3p	1.88	1.99E-02
miR-363-3p	1.66	2.29E-02
miR-374b-5p	2.41	3.17E-02
miR-20b-5p	1.91	3.28E-02
miR-223-3p	1.71	3.28E-02
miR-486-3p	1.55	3.56E-02
miR-195-5p	1.85	3.89E-02
miR-331-3p	1.80	3.89E-02
miR-26a-5p	2.02	3.99E-02
miR-16-5p	2.11	4.09E-02
miR-376a-3p	1.88	4.27E-02
miR-181a-5p	1.89	4.65E-02
miR-374a-5p	2.10	4.74E-02

Table S3: Differentially expressed miRNAs in acute respiratory distress patients, bacterial and viral lower respiratory tract infection vs viral infection alone. Significance tested by Wilcoxon's t-test (n=10 bacterial, n=9 viral).

miRNA	Fold Change	P-value
miR-192-5p	1.68	7.62E-03
miR-532-3p	1.88	1.01E-02
miR-486-3p	1.78	1.51E-02
miR-150-5p	1.98	1.72E-02
miR-let-7b-5p	2.03	2.20E-02
miR-548a-3p	-1.54	2.47E-02
miR-140-3p	1.39	2.79E-02
miR-215-5p	1.65	2.79E-02
miR-17-5p	1.40	3.50E-02
miR-324-3p	1.32	3.50E-02
miR-195-5p	1.63	4.35E-02
miR-486-5p	1.57	4.99E-02

Table S4: Differentially abundant metabolites acute respiratory distress vs control. Significance tested by t-test (n=4).

Metabolite	Median Abundance		Fold Change	P- value
	Control	ARDS		
5-Oxoproline	2.55E+06	4.59E+06	1.80E+00	2.31E-04
Glutamine	3.69E+06	6.36E+06	1.73E+00	5.98E-04
Taurine	1.77E+06	5.83E+06	3.29E+00	3.89E-03
N-Succinyl-L-citrulline	2.58E+05	4.81E+05	1.86E+00	1.91E-02
Glycerone phosphate	3.93E+07	4.75E+07	1.21E+00	2.65E-02
Leucine	2.95E+07	4.78E+07	1.62E+00	3.08E-02
L-Citrulline	1.51E+05	8.32E+05	5.50E+00	3.78E-02
Cysteine	1.14E+05	1.98E+05	1.74E+00	4.26E-02
UDP	2.34E+06	1.75E+06	7.47E-01	4.93E-02

Table S5: Significantly predicted pathways based on dysregulated miRNAs that include altered metabolites

Metabolites	Pathways	P-value	Q-value	miRNAs
5-oxoproline	Glutathione metabolism	9.40E-03	2.05E-02	hsa-miR-181a-5p; hsa-miR-16-5p; hsa-miR-186-5p; hsa-miR-125b-5p; hsa-miR-26a-5p; hsa-miR-195-5p; hsa-miR-331-3p; hsa-miR-142-3p
l-citrulline	Arginine biosynthesis	2.48E-02	4.24E-02	hsa-miR-181a-5p; hsa-miR-16-5p; hsa-miR-186-5p; hsa-miR-26a-5p; hsa-miR-142-3p
Taurine	Primary bile acid biosynthesis	3.72E-03	1.12E-02	hsa-miR-16-5p; hsa-miR-186-5p; hsa-miR-26a-5p; hsa-miR-142-3p
Taurine	ABC transporters	2.23E-04	3.15E-03	hsa-miR-181a-5p; hsa-miR-16-5p; hsa-miR-345-5p; hsa-miR-186-5p; hsa-miR-374a-5p; hsa-miR-125b-5p; hsa-miR-26a-5p; hsa-miR-195-5p; hsa-miR-374b-5p; hsa-miR-142-3p
Taurine	Neuroactive ligand-receptor interaction	6.70E-03	1.65E-02	hsa-miR-181a-5p; hsa-miR-16-5p; hsa-miR-375-3p; hsa-miR-345-5p; hsa-miR-186-5p; hsa-miR-374a-5p; hsa-miR-125b-5p; hsa-miR-26a-5p; hsa-miR-126-3p; hsa-miR-195-5p; hsa-miR-374b-5p; hsa-miR-331-3p; hsa-miR-142-3p; hsa-miR-139-5p
Glutamine	Arginine biosynthesis	2.48E-02	4.24E-02	hsa-miR-181a-5p; hsa-miR-16-5p; hsa-miR-186-5p; hsa-miR-26a-5p; hsa-miR-142-3p
Glutamine	Pyrimidine metabolism	1.00E-02	2.14E-02	hsa-miR-16-5p; hsa-miR-375-3p; hsa-miR-186-5p; hsa-miR-125b-5p; hsa-miR-26a-5p; hsa-miR-195-5p; hsa-miR-374b-5p; hsa-miR-331-3p; hsa-miR-142-3p
Glutamine	Vitamin B6 metabolism	1.33E-04	2.93E-03	hsa-miR-16-5p; hsa-miR-186-5p; hsa-miR-125b-5p; hsa-miR-26a-5p; hsa-miR-195-5p; hsa-miR-331-3p
Glutamine	Nitrogen metabolism	1.18E-03	6.04E-03	hsa-miR-16-5p; hsa-miR-186-5p; hsa-miR-374a-5p; hsa-miR-26a-5p; hsa-miR-195-5p; hsa-miR-374b-5p; hsa-miR-142-3p
Glutamine	ABC transporters	2.23E-04	3.15E-03	hsa-miR-181a-5p; hsa-miR-16-5p; hsa-miR-345-5p; hsa-miR-186-5p; hsa-miR-374a-5p; hsa-miR-125b-5p; hsa-miR-26a-5p; hsa-miR-195-5p; hsa-miR-374b-5p; hsa-miR-142-3p
Glutamine	Glutamatergic synapse	2.30E-03	8.68E-03	hsa-miR-181a-5p; hsa-miR-16-5p; hsa-miR-375-3p; hsa-miR-345-5p; hsa-miR-186-5p; hsa-miR-374a-5p; hsa-miR-125b-5p; hsa-miR-26a-5p; hsa-miR-126-3p; hsa-miR-195-5p; hsa-miR-374b-5p; hsa-miR-331-3p; hsa-miR-142-3p
Glutamine	GABAergic synapse	3.19E-03	1.03E-02	hsa-miR-181a-5p; hsa-miR-16-5p; hsa-miR-375-3p; hsa-miR-186-5p; hsa-miR-374a-5p; hsa-miR-125b-5p; hsa-miR-26a-5p; hsa-miR-195-5p; hsa-miR-374b-5p; hsa-miR-331-3p; hsa-miR-142-3p; hsa-miR-139-5p

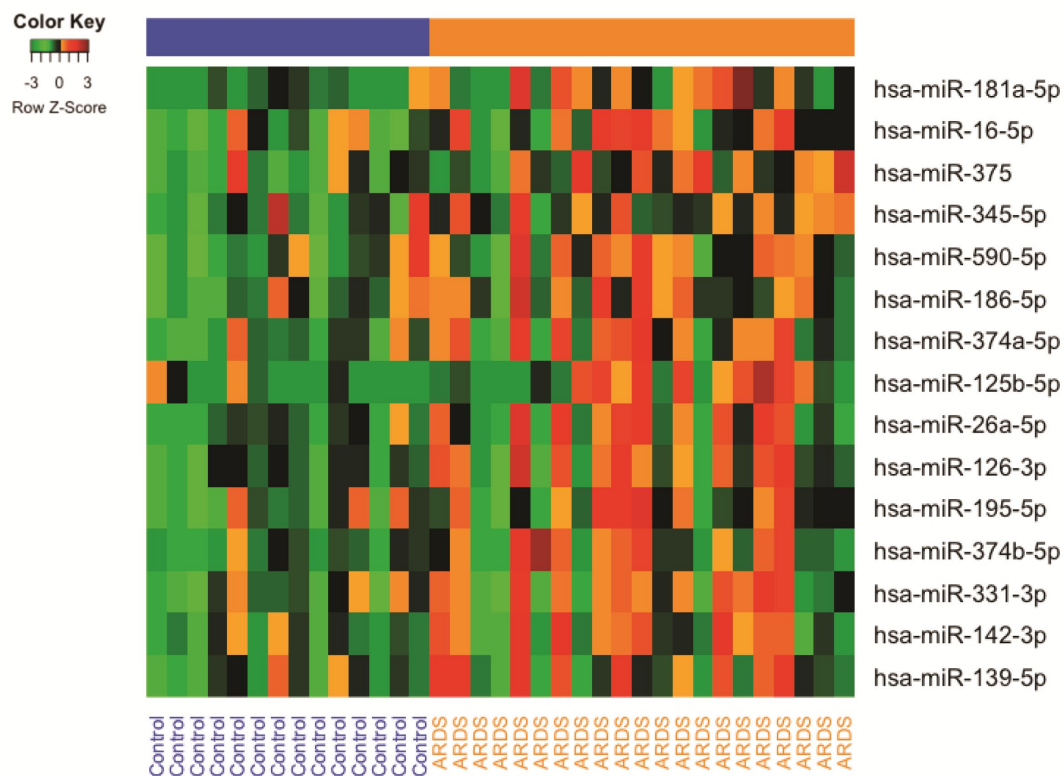


Fig S1: Differentially expressed microRNAs in ARDS vs control samples quantified by microarray. Fifteen microRNAs were differentially expressed ($p < 0.05$) by Wilcoxon rank sum test, $n=21$ ARDS, $n=14$ control. ARDS-Acute Respiratory Distress Syndrome.

Fig S2: Circos plot of correlations with a $p < 0.05$ and r value > 0.7 between miRNAs and metabolites.

