Supplementary Information

Distinct exosomal miRNA profiles from BALF and lung tissue from COPD and IPF patients

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Supplementary Tables

Supplementary Table S1: Significant Differentially expressed miRNAs in BALF exosomes.
derived

miRNA	log2foldchange	logCPM	pvalue	FDR	Functional Annotation
NS vs COPD					
hsa-miR-423-5p	-3.389204282	14.75498	0.0001336 9	0.0066	mRNA binding involved in posttranscriptional gene silencing. Role in apoptosis and cell proliferation
hsa-miR-320b	2.638473041	14.15853	0.0009897 8	0.0181 5	tumor suppressing role by targeting CDK6
hsa-miR-22-3p	2.508785494	18.34373	0.0002398 8	0.0066	negative regulator of endothelial cell proliferation and necroptotic process; but positive regulator of inflammatory response
Sm vs COPD					
hsa-miR-100-5p	-3.492285687	18.86802	3.29E-05	0.0015 8	negative regulation of cell differentiation and IL-8 secretion
NS vs IPF					
hsa-miR-200a-3p	-4.811568605	13.79069	7.88E-06	0.0001 4	positive regulator of blood vessel endothelial migration, role in Endothelial-mesenchymal transition
hsa-miR-141-3p	-4.31928888	11.4448	0.0004517 3	0.0042 2	positive regulator of cell proliferation and negative regulator of leukocyte adhesion to vascular endothelial cell

hsa-miR-375-3p	-4.255714743	12.47332	1.28E-05	0.00014	RNA polymerase II binding complex; positive regulator of endothelial cell apoptotic process
hsa-miR-423-5p	-3.37545635	14.95874	0.00376795	0.02416	mRNA binding involved in posttranscriptional gene silencing. Role in apoptosis and cell proliferation
hsa-miR-320b	3.186119102	14.24854	3.22E-06	9.03E-05	tumor suppressing role by targeting CDK6
hsa-miR-200b-3p	-2.849476778	14.33963	1.21E-05	0.00014	positive regulator of cell proliferation; negative regulator of gene expression
hsa-miR-22-3p	2.817552446	18.23789	3.10E-06	9.03E-05	negative regulator of endothelial cell proliferation and necroptotic process; but positive regulator of inflammatory response
hsa-miR-320a-3p	1.906370214	14.44337	0.00267282	0.02138	negative regulator of cell proliferation, cell migration and IL-4 biosynthetic process.
hsa-miR-24-3p	1.83111351	12.04935	0.00388364	0.02416	negative regulator of angiogenesis and blood vessel endothelial cell migration

<u>Supplementary Table S2:</u> Significant differentially expressed miRNAs in Lung-derived exosomes.

miRNA	log2foldchange	logCPM	pvalue	FDR	Function
NS vs COPD					
hsa-miR-122-5p	-3.081717764	8.0592	1.66E-05	0.00374	cell proliferation, migration, invasion, and EMT
Sm vs COPD					

hsa-miR-122-5p	-5.048802634	9.96494	1.64E-06	0.00033	cell proliferation, migration, invasion, and EMT
NS vs IPF					
hsa-miR-514a-3p	3.779748499	4.04505	3.15E-09	2.56E-07	Tumor suppressor
hsa-miR-506-3p	3.146428357	5.6144	4.98E-07	2.43E-05	negative regulator of cellular biosynthetic pathwaya and IL8 secretion
hsa-miR-21-5p	2.828829977	15.6156	2.70E-11	6.58E-09	negative modulator of angiogenesis; regulates extracellular matrix degradation
hsa-miR-338-5p	-2.821754174	8.55174	2.59E-09	2.56E-07	negative regulation of IL6 secretion and cell migration
hsa-miR-509-3p	2.767633188	5.4511	8.72E-05	0.00133	negative regulator of cell migration, invasion and proliferation
hsa-miR-223-3p	2.402273957	8.20475	1.88E-06	5.74E-05	negative regulator of GTPase activity and regulated macrophage differentiation
hsa-miR-30d-5p	-2.400812469	16.3117	8.89E-07	3.35E-05	regulates gene expression and EMT
hsa-miR-30d-3p	-2.22958366	5.29936	4.73E-05	0.00094	inhibitor of cell proliferation and invasion
hsa-miR-338-3p	-2.204598086	7.29224	9.62E-07	3.35E-05	negative regulator of cell migration and IL6 production
hsa-miR-30b-5p	-1.967255645	12.7584	1.59E-05	0.00039	positive regulator of TGF-beta signaling pathway, regulates lipid metabolism, association with senescence
hsa-miR-204-5p	-1.904426753	5.64924	5.69E-05	0.00099	negative regulation of IL6, IL1beta production and cell migration, regulates EMT
hsa-miR-122-5p	-1.822688383	8.34723	0.00025	0.00299	cell proliferation, migration, invasion, and EMT
hsa-miR-10b-5p	-1.754493357	13.4712	0.00202	0.01452	positive regulator of cell migration, Th17 regulator
hsa-miR-203a-3p	-1.740223733	10.5438	3.65E-05	0.00081	negative regulator of IL8 secretion, regulates EMT
hsa-miR-139-3p	-1.692253283	4.65751	0.00088	0.0077	Tumor suppressor, EMT

hsa-miR-486-5p	-1.636372182	13.0762	0.00604	0.03137	regulates gene expression and has been shown to be associated with IPF
hsa-miR-582-5p	1.590929655	3.94706	0.00196	0.01452	tumor suppressor
hsa-miR-21-3p	1.582268505	7.57847	0.00027	0.00299	negative modulator of angiogenesis; regulates extracellular matrix degradation
hsa-miR-379-5p	1.553371104	4.88324	0.00385	0.02409	negative regulator of cell proliferation and positive regulator of apoptosis
hsa-miR-132-3p	1.543109071	5.19083	0.00161	0.0128	negative regulator of gene expression, regulates inflammation and cell proliferation
hsa-miR-224-5p	-1.541206326	9.28135	1.55E-05	0.00039	regulates cell proliferation, migration and invasion through PIK3R3/Akt pathway
hsa-miR-144-5p	1.53599799	5.70304	0.00293	0.01932	negative regulator of EMT; positive regulation of mitochondrial organization
hsa-miR-889-3p	1.534772448	4.45827	0.00534	0.02833	regulates cell viability and invasion
hsa-miR-142-5p	1.514303487	8.17025	2.93E-08	1.79E-06	negative regulation of IL1beta, response to TNF
hsa-miR-7-5p	1.436816898	5.84014	0.00027	0.00299	inhibits cell migration and invasion, suppresses tumor metastasis
hsa-miR-1-3p	1.398003997	9.02882	0.00059	0.00551	cell proliferation and invasion
hsa-miR-424-3p	1.377444275	3.95708	0.00457	0.02718	negative regulation of cell proliferation and invasion, negative regulation of fibroblast growth factor receptor signaling
hsa-miR-10a-5p	-1.373153961	15.8906	0.00011	0.00157	cell migration and endothelial growth factor signaling
hsa-miR-125a-5p	-1.318243293	14.1273	0.00041	0.00397	fibroblast transdifferentiation, negative regulation of IL16
hsa-miR-106b-5p	1.308396822	4.51807	0.00325	0.02087	regulates EMT and TGF beta signaling, negative regulator of IL8
hsa-miR-23b-5p	-1.300249004	5.24808	0.00219	0.01524	TGF beta signaling regulation
hsa-miR-628-3p	-1.275911117	6.31838	0.00199	0.01452	regulator of cell proliferator

hsa-miR-181d-5p	-1.204679475	6.05627	0.00246	0.01669	inhibitor of cell proliferation and metastasis
hsa-miR-155-5p	1.199631772	7.4596	0.00163	0.0128	negative regulator of cytokine secretion and regulates epithelial barrier and EMT
hsa-miR-197-3p	-1.197907775	5.53844	0.00663	0.03303	negative regulation of IL-18
hsa-miR-183-5p	1.168387995	11.1446	4.99E-05	0.00094	TGF-beta signaling, positive regulation of phagocytosis
hsa-miR-126-5p	-1.161697617	10.4425	0.00028	0.00299	negative regulator of cell migration
hsa-miR-423-5p	-1.158386165	11.3123	0.00472	0.02741	negative regulator of cell invasion and migration
hsa-miR-589-5p	-1.113954446	5.58091	0.00416	0.0254	regulates EMT
hsa-miR-30a-5p	-1.077861429	14.4068	0.00017	0.00219	regulator of TGF-beta signaling
hsa-miR-144-3p	1.07056553	7.30821	0.00874	0.04023	negative regulator of EMT and positive regulator of mitochondrial organization
hsa-miR-199a-3p|hsa-miR-199b-3p	1.068687434	12.3784	0.00017	0.00219	positive regulator of endothelial cell migration, negative regulation of autophagy
hsa-miR-182-5p	1.0640442	11.2871	7.58E-05	0.00123	positive regulator of cell migration and cytokine secretion
hsa-miR-92a-3p	-1.061586028	11.5755	0.00486	0.02742	regulates TGF-beta signalling
hsa-miR-126-3p	-1.020449014	12.1275	0.00061	0.00551	role in angiogenesis and vascular homeostasis
hsa-miR-340-5p	0.968709958	7.35372	0.00494	0.02742	regulates cell proliferation
hsa-miR-409-3p	0.957771401	6.15189	0.01087	0.04821	promotes tumorigenesis
hsa-miR-30a-3p	-0.932099425	10.06	0.00107	0.00904	negative regulator of EMT
hsa-miR-146b-5p	0.920971946	15.3479	0.00797	0.03815	negative regulator of endothelial activation, EMT and IL17 pathway
hsa-miR-148a-3p	0.903657387	12.9195	0.00036	0.00362	role in tumor suppression
hsa-miR-342-3p	-0.890916332	9.21854	0.00834	0.03915	regulates TGF-beta signaling
hsa-miR-151b	-0.840780828	7.66417	0.0062	0.03153	represses cell migration
hsa-miR-103a-3p	0.80597023	9.14838	0.00769	0.03754	negative regulation of peptidyl-threonine

					phosphorylation, regulates glucose homeostasis
hsa-miR-186-5p	-0.734165882	11.605	0.00512	0.02778	regulates collagen and EMT
hsa-miR-151a-5p|hsa-miR-151b	-0.72411126	12.6144	0.00951	0.04297	regulates cell proliferation, migration and invasion

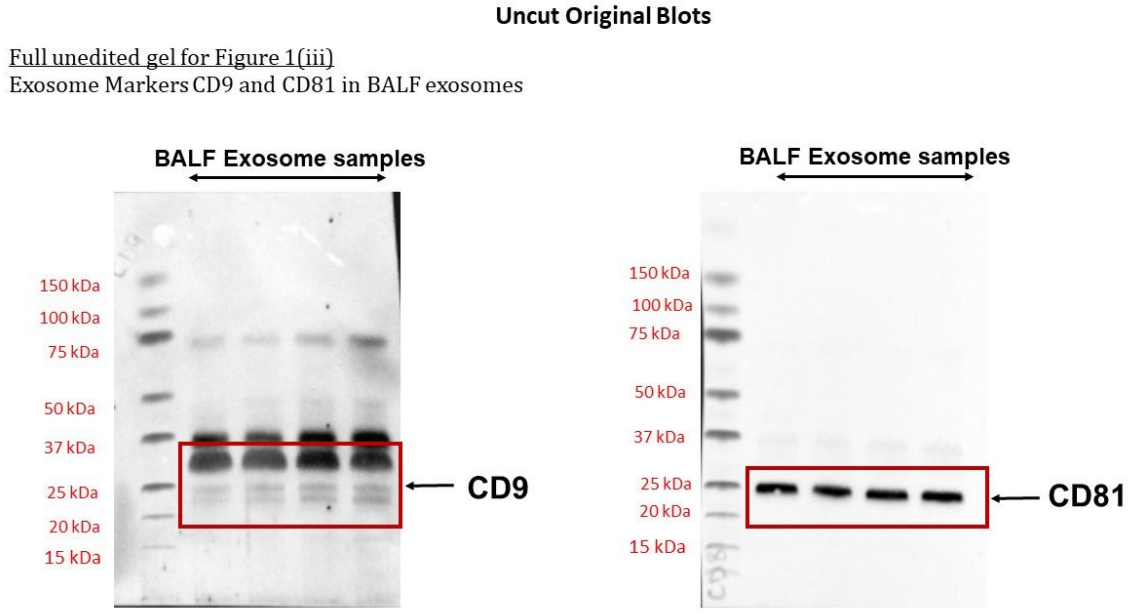
<u>Supplementary Table S3</u>: Significant differentially expressed miRNAs on comparing the miRNAs derived from BALF or Lung-derived exosomes from IPF vs COPD patients.

miRNAs	log2FoldChange	pvalue
BALF		
hsa-miR-375-3p	3.699215206	9.33E-05
Lung Tissues		
hsa-miR-10a-5p	1.409527466	1.74E-06
hsa-miR-99b-5p	0.849983751	0.0006781
hsa-miR-125a-5p	1.491008563	7.53E-05
hsa-miR-181a-5p	0.64855263	0.0039477
hsa-miR-21-5p	-2.735601026	1.21E-09
hsa-miR-125b-5p	0.928588863	0.0002024
hsa-miR-23a-3p	0.856645231	0.0034096
hsa-miR-199a-3p|hsa-miR-199b-3p	-0.816065829	0.0042361
hsa-miR-151a-5p|hsa-miR-151b	0.80742856	0.0024248
hsa-miR-92a-3p	1.120016981	0.0023208
hsa-miR-182-5p	-1.034019544	0.0002701
hsa-miR-221-5p	0.751510707	0.0041159
hsa-miR-145-5p	0.792259796	0.0053713
hsa-miR-342-3p	1.28928554	1.01E-05
hsa-miR-103a-3p	-0.886227511	0.0037171
hsa-miR-224-5p	1.033150905	0.0025444
hsa-miR-338-5p	2.10636214	2.35E-06
hsa-miR-338-3p	1.324111402	0.0046041
hsa-miR-429	-1.35855317	0.0056567
hsa-miR-1-3p	-1.341960391	0.000599
hsa-miR-142-5p	-1.323394065	4.86E-08
hsa-miR-484	0.875965255	0.0053921
hsa-miR-151b	0.813176399	0.0020734
hsa-miR-340-5p	-1.386800711	9.40E-06

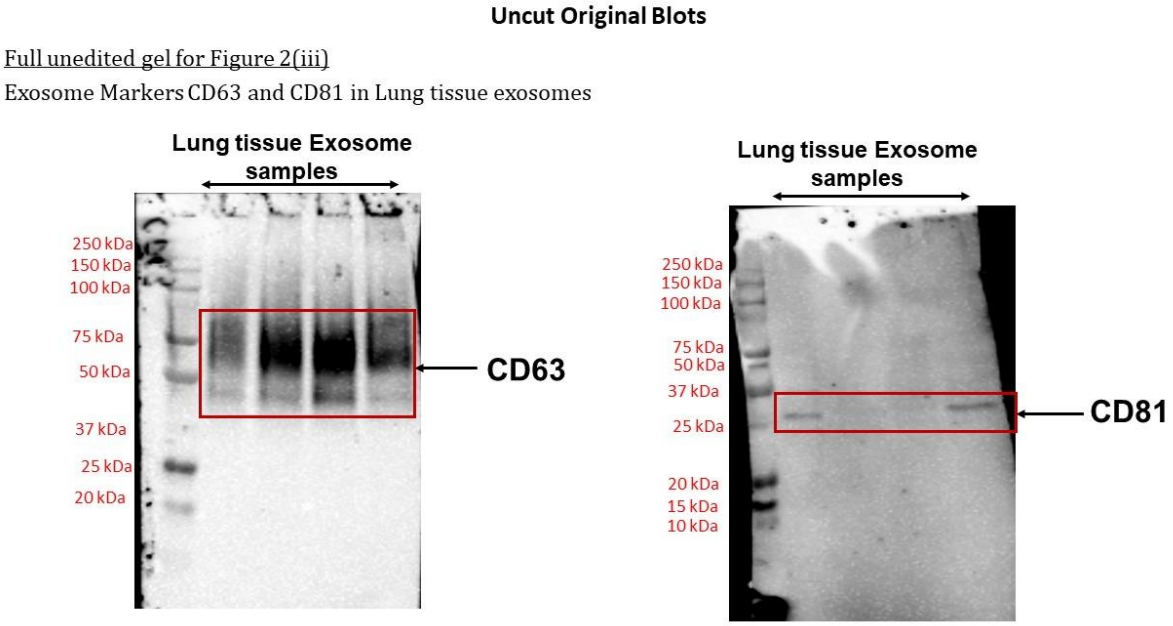
hsa-miR-223-3p	-3.347367864	1.96E-14
hsa-miR-374a-5p	-1.512435161	7.90E-05
hsa-miR-1271-5p	1.294527177	0.000127
hsa-miR-374a-3p	-1.32118481	0.0002536
hsa-miR-365a-3p|hsa-miR-365b-3p	1.255379081	0.0005726
hsa-miR-181d-5p	1.006691821	0.0032183
hsa-miR-205-5p	-1.744538429	0.0032418
hsa-miR-197-3p	1.883112149	1.55E-08
hsa-miR-21-3p	-1.491535768	0.0055195
hsa-miR-204-5p	1.232430302	0.0020586
hsa-miR-345-5p	-1.251470622	0.0001833
hsa-miR-23b-5p	1.489623445	0.0005267
hsa-miR-107	-0.870195285	0.0056404
hsa-miR-32-5p	-1.49781331	0.0038593
hsa-miR-139-3p	1.549991658	0.0003531
hsa-miR-24-2-5p	-1.705632668	0.0002179
hsa-miR-328-3p	1.448057593	0.0013465
hsa-miR-22-5p	-1.413680584	0.003023
hsa-miR-142-3p	-2.681623009	2.97E-05
hsa-miR-548e-3p	-1.185559978	0.0033579
hsa-miR-424-5p	-2.000054742	0.0038114
hsa-miR-889-3p	-1.595329766	0.0022859
hsa-miR-135b-5p	-1.860676506	0.0033555
hsa-miR-381-3p	-1.47381252	0.0014309
hsa-miR-3613-3p	2.375696693	0.0035104
hsa-miR-223-5p	-3.145005297	0.0001399
hsa-miR-3613-5p	-3.686449059	4.50E-07
hsa-miR-508-3p	-2.637539744	0.0035568
hsa-miR-708-5p	-2.487002959	0.0011469
hsa-miR-3130-3p	-3.482486124	0.0013965
hsa-miR-31-5p	-3.475504137	2.37E-05
hsa-miR-377-3p	-3.248729824	3.06E-06
hsa-miR-514a-3p	-2.611946541	0.0014603
hsa-miR-369-3p	-2.604592827	0.0020431
hsa-miR-4732-3p	4.179938703	0.0038075
hsa-miR-449a	-3.994764171	0.0025207
hsa-miR-4683	4.884780183	1.98E-05
hsa-miR-1291	2.949952436	0.0031089
hsa-miR-7977	4.359794794	1.89E-05
hsa-miR-656-3p	-2.054137869	0.0051107
hsa-miR-4738-3p	4.411823484	0.0001546

hsa-miR-6892-5p	2.760729508	0.0036942
hsa-miR-1277-5p	-5.967010493	0.0010824

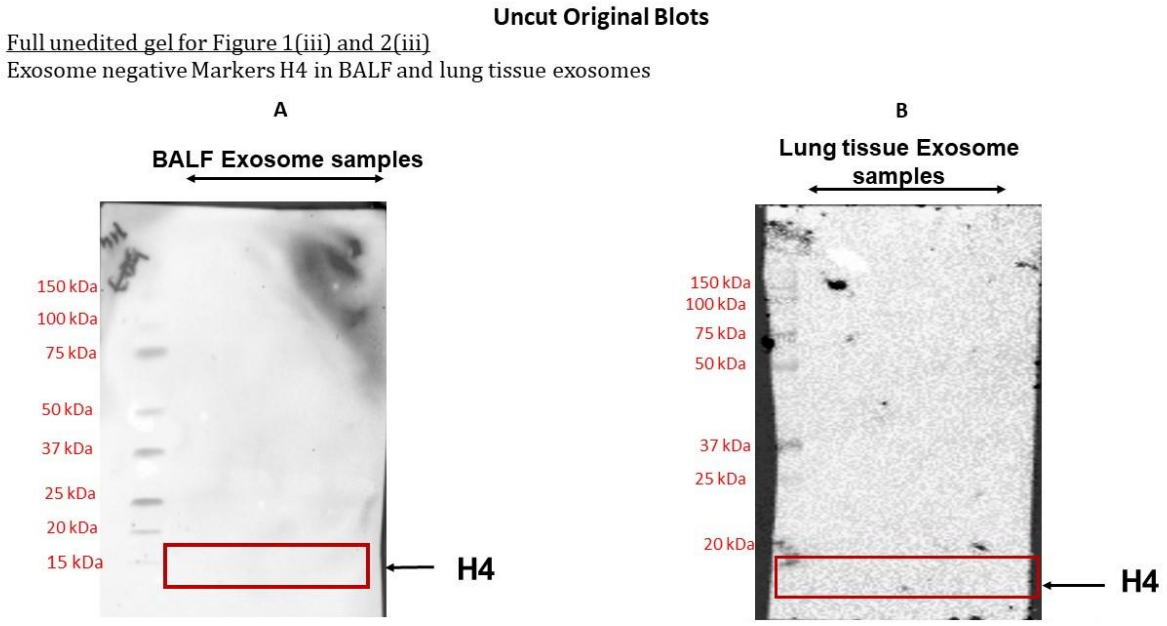
Supplementary Figures



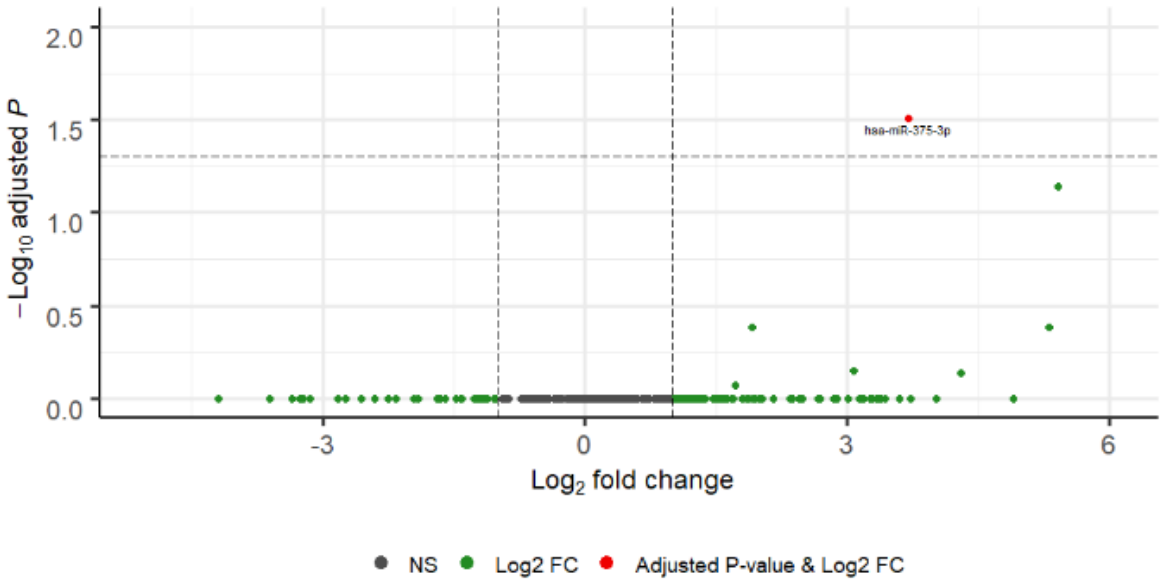
Supplementary Figure S1: Figure showing the original uncut blots for CD9 and CD81from BALF exosome fraction as shown in Figure 1(iii) of the manuscript.



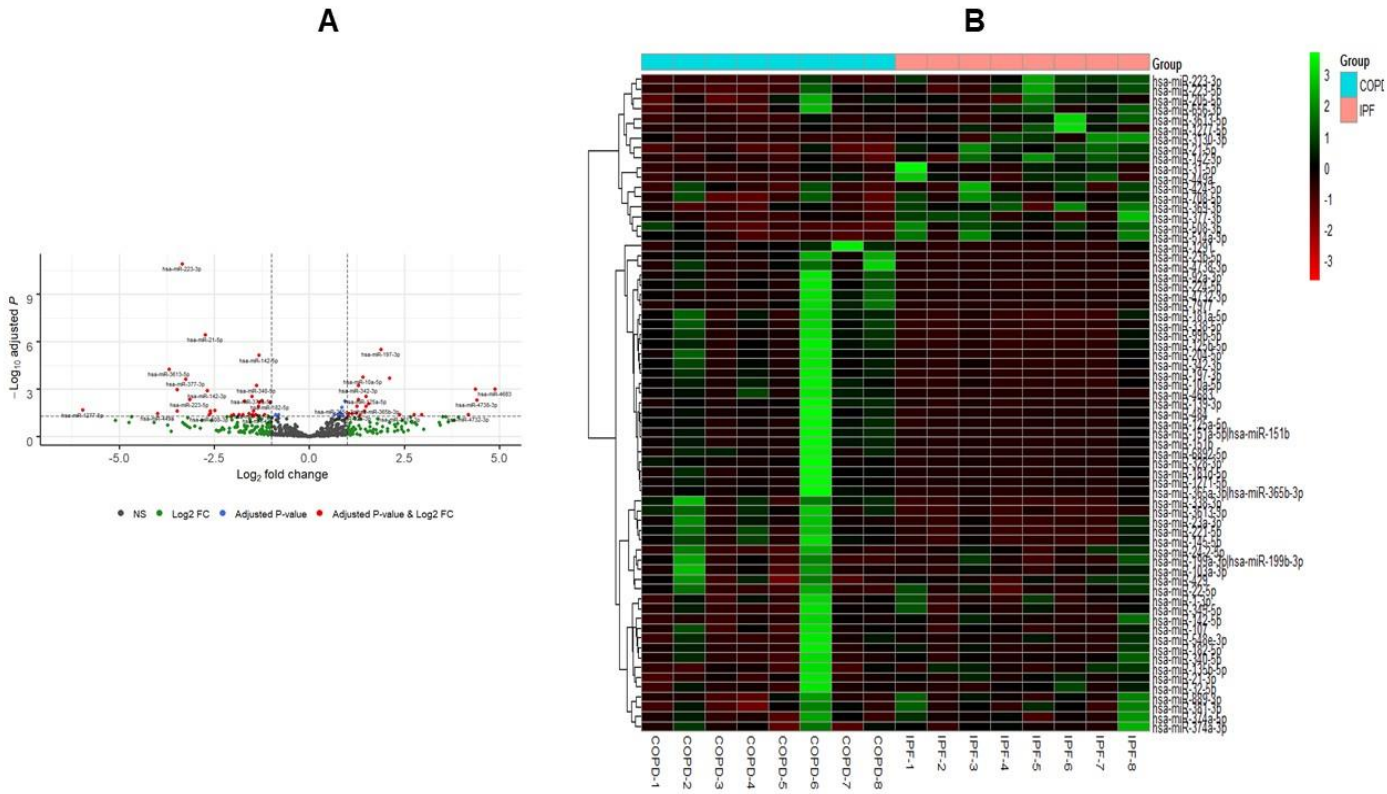
Supplementary Figure S2: Figure showing the original uncut blots for CD63 and CD81from lung tissue exosome fraction as shown in Figure 2(iii) of the manuscript.



Supplementary Figure S3: Figure showing the original uncut blots for negative exosomal marker (H4) from (A) BALF and (B) lung tissue-derived exosome fraction as shown in Figures 1(iii) and 2(iii) respectively of the manuscript. NOTE: The blot probed for CD9 for BALF exosomes was stripped and re-probed for H4.



Supplementary Figure S4: Volcano plot showing differentially expressed miRNAs amongst BALF-derived exosomes from IPF vs COPD patients.



Supplementary Figure S5: (A) Volcano plot and (B) Heat map showing differentially expressed miRNAs amongst Lung tissue-derived exosomes from IPF vs COPD patients.