

Supporting Information

Proteomic Analysis of Plasma-derived Extracellular Vesicles in Smokers and Patients with Chronic Obstructive Pulmonary Disease

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Table S1. GO enrichment analysis for EV markers identified in this study that are common among Top 100 EV markers present in Vesiclepedia analyzed by STRING database.

Biological Process (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0042060	Wound healing	15	8.12E-12
GO:0002576	Platelet degranulation	9	1.07E-11
GO:0030168	Platelet activation	11	1.54E-11
GO:0050878	Regulation of body fluid levels	14	4.65E-11
GO:0007596	Blood coagulation	12	1.61E-09

Molecular Function (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0005515	Protein binding	24	1.61E-09
GO:0003723	RNA binding	14	2.92E-06
GO:0044822	Poly(A) RNA binding	12	1.24E-05
GO:0032403	Protein complex binding	9	1.76E-05
GO:0008092	Cytoskeletal protein binding	8	0.000156

Cellular Component (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0070062	Extracellular exosome	28	4.76E-23
GO:0005576	Extracellular region	28	5.71E-18
GO:0072562	Blood microparticle	10	1.99E-14
GO:0005925	Focal adhesion	12	2.4E-12
GO:0005615	Extracellular space	16	3.24E-11

KEGG Pathways			
Pathway ID	Pathway description	Count in gene set	False discovery rate
04810	Regulation of actin cytoskeleton	6	9.22E-05
05132	Salmonella infection	4	0.000416
05203	Viral carcinogenesis	5	0.000416
04510	Focal adhesion	5	0.000524
00010	Glycolysis / Gluconeogenesis	3	0.00428

Table S2. GO enrichment analysis for EV markers identified in this study that are common among Top 100 Exosomal markers present in ExoCarta analyzed by STRING database.

Biological Process (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0030168	Platelet activation	9	2.14E-08
GO:0002576	Platelet degranulation	7	2.66E-08
GO:0042060	Wound healing	11	1.14E-07
GO:0016192	Vesicle-mediated transport	12	6.93E-07
GO:0050878	Regulation of body fluid levels	10	1.35E-06

Molecular Function (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0005515	Protein binding	21	3.44E-09
GO:0003723	RNA binding	14	8.37E-08
GO:0044822	Poly(A) RNA binding	12	7.09E-07
GO:1901363	Heterocyclic compound binding	19	1.13E-05
GO:0097159	Organic cyclic compound binding	19	1.14E-05

Cellular Component (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0070062	Extracellular exosome	23	1.37E-18
GO:0005576	Extracellular region	23	1.79E-14
GO:0043209	Myelin sheath	9	9.37E-12
GO:0005925	Focal adhesion	9	1.39E-08
GO:0042470	Melanosome	6	1.06E-07

KEGG Pathways			
Pathway ID	Pathway description	Count in gene set	False discovery rate
05132	Salmonella infection	4	0.000547
04145	Phagosome	4	0.00255
00010	Glycolysis / Gluconeogenesis	3	0.0039

Table S3. GO enrichment analysis for EV markers identified in this study that are common among EV markers present in Plasma Proteome Database analyzed by STRING database.

Biological Process (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0072376	Protein activation cascade	31	2.14E-49
GO:0006956	Complement activation	24	7.68E-40
GO:0002576	Platelet degranulation	25	5.37E-33
GO:0006950	Response to stress	78	1.12E-32
GO:0016192	Vesicle-mediated transport	51	4.41E-31

Molecular Function (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0004866	Endopeptidase inhibitor activity	19	1.33E-16
GO:0061134	Peptidase regulator activity	20	1.33E-16
GO:0005515	Protein binding	64	1.35E-12
GO:0004857	Enzyme inhibitor activity	20	2.13E-12
GO:0004867	Serine-type endopeptidase inhibitor activity	12	9.69E-11

Cellular Component (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0072562	Blood microparticle	71	3.43E-104
GO:0005615	Extracellular space	87	8.74E-79
GO:0044421	Extracellular region part	107	5.52E-67
GO:0070062	Extracellular exosome	98	5.38E-65
GO:0005576	Extracellular region	109	8.24E-63

KEGG Pathways			
Pathway ID	Pathway description	Count in gene set	False discovery rate
04610	Complement and coagulation cascades	31	2.84E-50
05150	Staphylococcus aureus infection	14	3.16E-18
05322	Systemic lupus erythematosus	11	6.46E-10
05133	Pertussis	9	1.58E-08
05020	Prion diseases	6	3.15E-06

Table S6. GO enrichment analysis for peptides identified in this study that are significantly different among non-smokers vs. smokers analyzed by STRING database.

Biological Process (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0045861	Negative regulation of proteolysis	8	2.21E-06
GO:0010951	Negative regulation of endopeptidase activity	7	2.31E-06
GO:0051346	Negative regulation of hydrolase activity	8	2.31E-06
GO:0051248	Negative regulation of protein metabolic process	10	3.79E-06
GO:0030162	Regulation of proteolysis	9	5.51E-06

Molecular Function (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0004866	Endopeptidase inhibitor activity	7	7.58E-08
GO:0004867	Serine-type endopeptidase inhibitor activity	5	8.75E-06
GO:0008201	Heparin binding	5	7.54E-05
GO:0001848	Complement binding	2	0.0179
GO:0005319	Lipid transporter activity	3	0.0179

Cellular Component (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0005615	Extracellular space	17	2.65E-17
GO:0072562	Blood microparticle	8	1.36E-11
GO:0070062	Extracellular exosome	16	1.88E-10
GO:0005576	Extracellular region	17	3.63E-09
GO:0034358	Plasma lipoprotein particle	4	3.71E-06

KEGG Pathways			
Pathway ID	Pathway description	Count in gene set	False discovery rate
4610	Complement and coagulation cascades	5	8.31E-07

Table S7. GO enrichment analysis for peptides identified in this study that are significantly different among smokers vs. COPD analyzed by STRING database.

Biological Process (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0010951	Negative regulation of endopeptidase activity	7	2.43E-05
GO:0051346	Negative regulation of hydrolase activity	8	2.43E-05
GO:0052548	Regulation of endopeptidase activity	8	2.43E-05
GO:1903034	Regulation of response to wounding	8	2.43E-05
GO:0032102	Negative regulation of response to external stimulus	6	0.000441

Molecular Function (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0004866	Endopeptidase inhibitor activity	7	1.09E-06
GO:0008201	Heparin binding	5	0.000629
GO:0004857	enzyme inhibitor activity	6	0.00147

Cellular Component (GO)			
Pathway ID	Pathway description	Count in gene set	False discovery rate
GO:0005615	Extracellular space	22	1.90E-21
GO:0072562	Blood microparticle	10	2.26E-14
GO:0070062	Extracellular exosome	20	1.03E-11
GO:0031988	Membrane-bounded vesicle	21	2.05E-11
GO:0005576	Extracellular region	22	8.73E-11

KEGG Pathways			
Pathway ID	Pathway description	Count in gene set	False discovery rate
4610	Complement and coagulation cascades	6	5.21E-08
5150	Staphylococcus aureus infection	3	0.00463
5133	Pertussis	3	0.00766