A

Sample	Number of proteins
HC1	266
HC2	328
HC3	414
P1	419
P2	356
P3	395
P4	362
P5	436
P6	383

B

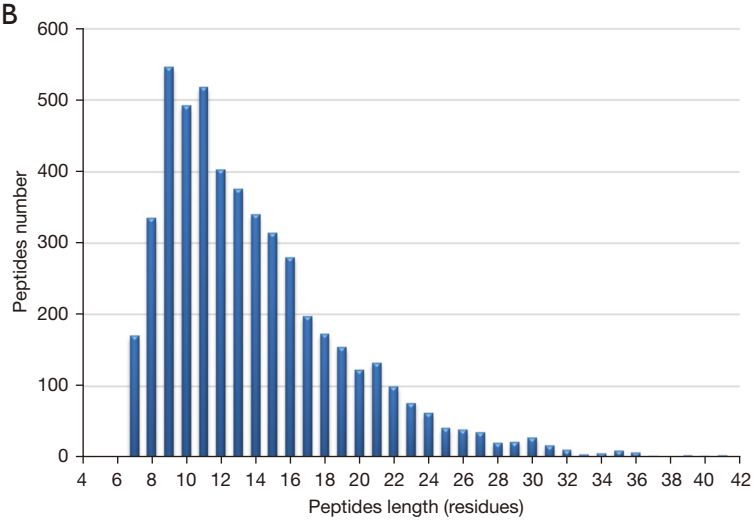

Figure S1 Proteomic analysis of serum sEV. (A) The number of proteins in the three healthy children and children with pneumonia. (B) Spectral counts of all peptides. HC, healthy control; P, pneumonia; sEV, small extracellular vesicle.

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Table S1 GSEA analysis of GO biological process of 180 proteins

ID	Description	Enrichment score	NES	P value	P.adjust	q values	Core enrichment
GO:0002449	Lymphocyte mediated immunity	0.521	1.892	0.002	0.026	0.018	IGLV6-57, C1R, C4A, C3, C7, IGHG3, IGHG1, CLU, IGHV5-51, C4BPB, HPX, IGLV3-25, IGHG2, IGHV4-61, IGHV3-49, C4BPA
GO:0002460	Adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	0.521	1.892	0.002	0.026	0.018	IGLV6-57, C1R, C4A, C3, C7, IGHG3, IGHG1, CLU, IGHV5-51, C4BPB, HPX, IGLV3-25, IGHG2, IGHV4-61, IGHV3-49, C4BPA
GO:0006950	Response to stress	0.475	1.830	0.002	0.026	0.018	SERPINA1, PROS1, C1R, C4A, C3, SERPINC1, C7, F2, CFH, ITGB3, ITIH4, VTN, IGHG3, IGHG1, SAA4, CLU, IGHV5-51, HP, C4BPB, MMRN1, HPX, ORM1, IGHG2, IGHV4-61, IGHV3-49, ORM2, C4BPA, GSN, F11, PF4, FGG, AHSG, FLNA, IGHA1, LRP1, HBB, TF, MYH9, FBLN1, FCN3, FGB, IGKC, IGHV3-73
GO:0006956	Complement activation	0.549	2.021	0.002	0.026	0.018	IGLV6-57, PROS1, C1R, C4A, C3, C7, F2, CFH, VTN, IGHG3, IGHG1, CLU, IGHV5-51, C4BPB, IGLV3-25, IGHG2, IGHV4-61, IGHV3-49, C4BPA
GO:0048856	Anatomical structure development	–0.446	–1.650	0.002	0.026	0.018	VCAN, GNB1, HSPB1, CSTA, TYMP, SSC5D, HEG1, HRG, FMN2, GLIPR2, THBS4, COL4A2, MSN, S100A7, CALM3, CALML5, COL4A1, HMGB1, ANXA2, PRDX2, COL1A2, COL1A1, DSC1, COL2A1, DSG1, HAPLN1, CASP14, ACAN, DSP
GO:0002455	Humoral immune response mediated by circulating immunoglobulin	0.565	2.011	0.002	0.026	0.018	IGLV6-57, C1R, C4A, C3, C7, IGHG3, IGHG1, CLU, IGHV5-51, C4BPB, HPX, IGLV3-25, IGHG2, IGHV4-61, IGHV3-49, C4BPA
GO:0009605	Response to external stimulus	0.445	1.693	0.002	0.026	0.018	PROS1, C1R, C4A, C3, SERPINC1, C7, F2, CFH, ITGB3, VTN, IGHG3, IGHG1, CLU, IGHV5-51, HP, C4BPB, HPX, IGHG2, IGHV4-61, IGHV3-49, C4BPA, GSN, F11, PF4, FGG, AHSG, FLNA, IGHA1, LRP1, TF
GO:0016064	Immunoglobulin mediated immune response	0.565	2.011	0.002	0.026	0.018	IGLV6-57, C1R, C4A, C3, C7, IGHG3, IGHG1, CLU, IGHV5-51, C4BPB, HPX, IGLV3-25, IGHG2, IGHV4-61, IGHV3-49, C4BPA
GO:0019724	B cell mediated immunity	0.565	2.011	0.002	0.026	0.018	IGLV6-57, C1R, C4A, C3, C7, IGHG3, IGHG1, CLU, IGHV5-51, C4BPB, HPX, IGLV3-25, IGHG2, IGHV4-61, IGHV3-49, C4BPA
GO:0002697	Regulation of immune effector process	0.615	2.156	0.002	0.026	0.018	IGLV6-57, PROS1, C1R, C4A, C3, C7, F2, CFH, VTN, IGHG3, IGHG1, CLU, C4BPB, HPX, IGLV3-25, IGHG2, C4BPA

Table S1 (*continued*)

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Table S1 (*continued*)

ID	Description	Enrichment score	NES	P value	P.adjust	q values	Core enrichment
GO:0048518	Positive regulation of biological process	0.426	1.638	0.002	0.026	0.018	IGLV6-57, PROS1, C1R, C4A, C3, C7, F2, CFH, ITGB3, VTN, IGHG3, IGHG1, CLU, IGHV5-51, HP, C4BPB, HPX, IGLV3-25, ORM1, IGHG2, IGHV4-61, IGHV3-49, ORM2, C4BPA, GSN, F11, PF4, FGG, AHSG, FLNA, IGHA1, LRP1, HBB, TF, IGLV3-27, MYH9, FBLN1, FCN3, FGB, IGKC, IGHV3-73
GO:0002920	Regulation of humoral immune response	0.663	2.275	0.002	0.026	0.018	IGLV6-57, PROS1, C1R, C4A, C3, C7, F2, CFH, VTN, IGHG3, IGHG1, CLU, C4BPB, HPX, IGLV3-25, IGHG2, C4BPA
GO:0006958	Complement activation, classical pathway	0.546	1.934	0.002	0.026	0.018	IGLV6-57, C1R, C4A, C3, C7, IGHG3, IGHG1, CLU, IGHV5-51, C4BPB, IGLV3-25, IGHG2, IGHV4-61, IGHV3-49, C4BPA
GO:0002253	Activation of immune response	0.523	1.920	0.002	0.026	0.018	IGLV6-57, PROS1, C1R, C4A, C3, C7, F2, CFH, VTN, IGHG3, IGHG1, CLU, IGHV5-51, C4BPB, IGLV3-25, IGHG2, IGHV4-61, IGHV3-49, C4BPA
GO:0030449	Regulation of complement activation	0.648	2.224	0.002	0.026	0.018	IGLV6-57, PROS1, C1R, C4A, C3, C7, F2, CFH, VTN, IGHG3, IGHG1, CLU, C4BPB, IGLV3-25, IGHG2, C4BPA
GO:0050778	Positive regulation of immune response	0.518	1.943	0.002	0.026	0.018	IGLV6-57, PROS1, C1R, C4A, C3, C7, F2, CFH, VTN, IGHG3, IGHG1, CLU, IGHV5-51, C4BPB, HPX, IGLV3-25, IGHG2, IGHV4-61, IGHV3-49, C4BPA
GO:0048513	Animal organ development	–0.609	–2.009	0.002	0.026	0.018	MSN, S100A7, CALM3, COL4A1, HMGB1, ANXA2, PRDX2, COL1A2, COL1A1, DSC1, COL2A1, DSG1, CASP14, DSP
GO:0006952	Defense response	0.496	1.869	0.002	0.026	0.018	SERPINA1, C1R, C4A, C3, SERPINC1, C7, F2, CFH, ITIH4, IGHG3, IGHG1, SAA4, CLU, IGHV5-51, HP, C4BPB, HPX, ORM1, IGHG2, IGHV4-61, IGHV3-49, ORM2, C4BPA, GSN, PF4, AHSG, FLNA, IGHA1
GO:0007275	Multicellular organism development	–0.471	–1.688	0.002	0.026	0.018	VCAN, GNB1, HSPB1, CSTA, TYMP, SSC5D, HEG1, HRG, FMN2, GLIPR2, THBS4, COL4A2, MSN, S100A7, CALM3, COL4A1, HMGB1, ANXA2, PRDX2, COL1A2, COL1A1, DSC1, COL2A1, DSG1, HAPLN1, CASP14, ACAN, DSP
GO:0048731	System development	–0.496	–1.759	0.002	0.026	0.018	COL4A2, MSN, S100A7, CALM3, COL4A1, HMGB1, ANXA2, PRDX2, COL1A2, COL1A1, DSC1, COL2A1, DSG1, HAPLN1, CASP14, ACAN, DSP
GO:0045861	Negative regulation of proteolysis	0.639	1.851	0.002	0.026	0.018	SERPINA1, PROS1, C4A, C3, SERPINC1, F2, ITIH4, VTN
GO:0032502	Developmental process	–0.436	–1.633	0.004	0.047	0.033	COL4A2, MSN, S100A7, CALM3, CALML5, COL4A1, HMGB1, ANXA2, PRDX2, COL1A2, COL1A1, DSC1, COL2A1, DSG1, HAPLN1, CASP14, ACAN, DSP

GSEA, gene set enrichment analysis; GO, Gene Ontology.

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Table S2 GO biological processes enrichment analysis of 10 unique proteins in the pneumonia group

Term name	Term ID	Adjusted P value	Negative log10 of adjusted P value	Intersections
Response to lipopolysaccharide	GO:0032496	0.0110048	1.95841795	LBP, DEFA3, MPO, DCN
Respiratory burst involved in defense response	GO:0002679	0.0110048	1.95841795	LBP, MPO
Response to molecule of bacterial origin	GO:0002237	0.0110048	1.95841795	LBP, DEFA3, MPO, DCN
Response to lipid	GO:0033993	0.01759282	1.75466446	LBP, DEFA3, MPO, DCN, ACTA1
Plasma lipoprotein particle remodeling	GO:0034369	0.01759282	1.75466446	PLTP, MPO
Protein-lipid complex remodeling	GO:0034368	0.01759282	1.75466446	PLTP, MPO
Respiratory burst	GO:0045730	0.01759282	1.75466446	LBP, MPO
Protein-containing complex remodeling	GO:0034367	0.01759282	1.75466446	PLTP, MPO
Response to mechanical stimulus	GO:0009612	0.02031912	1.69209504	MPO, DCN, ACTA1
Defense response to fungus	GO:0050832	0.02031912	1.69209504	DEFA3, MPO
Positive regulation of cytolysis	GO:0045919	0.02407622	1.6184117	LBP
Protein-lipid complex subunit organization	GO:0071825	0.02407622	1.6184117	PLTP, MPO
Plasma lipoprotein particle organization	GO:0071827	0.02407622	1.6184117	PLTP, MPO
Response to gold nanoparticle	GO:1990268	0.02407622	1.6184117	MPO
Vitamin E biosynthetic process	GO:0010189	0.02407622	1.6184117	PLTP
Response to fungus	GO:0009620	0.02407622	1.6184117	DEFA3, MPO
Hypochlorous acid biosynthetic process	GO:0002149	0.02407622	1.6184117	MPO
Hypochlorous acid metabolic process	GO:0002148	0.02407622	1.6184117	MPO
Opsonization	GO:0008228	0.02612928	1.58287262	LBP, IGLV2-11
Response to bacterium	GO:0009617	0.02612928	1.58287262	LBP, DEFA3, MPO, DCN
Response to external stimulus	GO:0009605	0.02612928	1.58287262	LBP, IGLV2-11, DEFA3, MPO, DCN, GP1BA, ACTA1
Positive regulation of respiratory burst involved in inflammatory response	GO:0060265	0.03295295	1.48210573	LBP
Defense response to Gram-negative bacterium	GO:0050829	0.03295295	1.48210573	LBP, DEFA3
Carbohydrate derivative transport	GO:1901264	0.03295295	1.48210573	LBP, PLTP
Response to transition metal nanoparticle	GO:1990267	0.03295295	1.48210573	MPO
Defense response to bacterium	GO:0042742	0.03295295	1.48210573	LBP, DEFA3, MPO
Lipopolysaccharide transport	GO:0015920	0.03295295	1.48210573	LBP
Humoral immune response	GO:0006959	0.0347306	1.45928776	IGLV2-11, CPN2, DEFA3
Immune system process	GO:0002376	0.03476081	1.45891015	LBP, IGLV2-11, CPN2, PDIA3, DEFA3, MPO, GP1BA
Peptide cross-linking	GO:0018149	0.0352354	1.45302085	IGLV2-11, DCN
Defense response to Gram-positive bacterium	GO:0050830	0.03844169	1.41519748	LBP, DEFA3
Regulation of plasma lipoprotein particle levels	GO:0097006	0.03923814	1.40629161	PLTP, MPO

Table S2 (*continued*)

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Table S2 (*continued*)

Term name	Term ID	Adjusted P value	Negative log10 of adjusted P value	Intersections
Regulation of immune effector process	GO:0002697	0.03923814	1.40629161	LBP, IGLV2-11, CPN2
Regulation of cytolysis	GO:0042268	0.03923814	1.40629161	LBP
Regulation of complement activation	GO:0030449	0.0395224	1.40315672	IGLV2-11, CPN2
Skeletal muscle fiber adaptation	GO:0043503	0.04558035	1.3412223	ACTA1
Vitamin E metabolic process	GO:0042360	0.04558035	1.3412223	PLTP
Response to yeast	GO:0001878	0.04558035	1.3412223	MPO

GO, Gene Ontology.

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