

Title:**Pangolin scales as adaptations for innate immunity against pathogens****Authors:**

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Supplementary Tables

Table S1: A list of sequences used in this study

No.	Accession Number	Scientific Name	Common Name/Strain	Analysis	Geographical Origin	Remarks
1	GCA_001685135.1	<i>Manis javanica</i>	Malayan pangolin	Metagenomic analysis	Malaysia	Used as a reference genome of pangolin
2	NZ_CP021058.1	<i>Macrococcus caseolyticus</i>	IMD0819	Metagenomic analysis	-	Used to reconstruct bacterial genome and calculate genome completeness.
3	NZ_KB849702.1	<i>Acinetobacter johnsonii</i>	ANC 3681	Metagenomic analysis	-	Used to reconstruct bacterial genome and calculate genome completeness.
4	NZ_CP016990.1	<i>Aeromonas hydrophila</i>	ZYAH75	Metagenomic analysis	-	Used to reconstruct bacterial genome and calculate genome completeness.

5	NZ_CP013990.1	<i>Leclercia adecarboxylata</i>	USDA-ARS- USMARC-60222	Metagenomic analysis	-	Used to reconstruct bacterial genome and calculate genome completeness.
6	NZ_CP021058.1	<i>Macrococcus caseolyticus</i>	IMD0819	Metagenomic analysis	-	Used to reconstruct bacterial genome and calculate genome completeness.
7	NZ_LS483441.1	<i>Aeromonas caviae</i>	NCTC12244	Metagenomic analysis	-	Used to reconstruct bacterial genome and calculate genome completeness.
8	KP261029.1	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	Thailand	
9	KP261030.1	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	South-East Asia	
10	KP261031.1	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	South-East Asia	
11	MJ5 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	Malaysia	This Cytb sequence was obtained from the internal

						database of the Department of Wildlife and National Parks (DWNP), Peninsular Malaysia
12	MJ6 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	Malaysia	This Cytb sequence was obtained from the internal database of the Department of Wildlife and National Parks (DWNP), Peninsular Malaysia
13	MJ7 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	Malaysia	This Cytb sequence was obtained from the internal database of the Department of Wildlife and National Parks (DWNP), Peninsular Malaysia
14	DS2 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	South-East Asia	This Cytb sequence was obtained from our internal database. It was extracted from the processed scale bought at

						pharmaceutical company in China
15	DS3 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	South-East Asia	This Cytb sequence was obtained from our internal database. It was extracted from the processed scale bought at pharmaceutical company in China
16	CS1 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	South-East Asia	
17	CS2 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	South-East Asia	
18	CS3 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	South-East Asia	
19	CS4 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	South-East Asia	

20	CS5 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	South-East Asia
21	CS6 (internal ID)	<i>Manis javanica</i>	Malayan pangolin	Phylogenetic analysis	South-East Asia
22	AJ304500.1	<i>Manis pentadactyla</i>	Chinese pangolin	Phylogenetic analysis	Taiwan
23	KP261033.1	<i>Manis pentadactyla</i>	Chinese pangolin	Phylogenetic analysis	South-East Asia
24	KP261032.1	<i>Manis pentadactyla</i>	Chinese pangolin	Phylogenetic analysis	South-East Asia
25	KP261034.1	<i>Manis pentadactyla</i>	Chinese pangolin	Phylogenetic analysis	South-East Asia
26	KJ123729.1	<i>Manis crassicaudata</i>	Indian pangolin	Phylogenetic analysis	India
27	KJ193405.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa

28	KJ193406.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
29	KJ193399.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
30	KJ193398.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
31	KJ193397.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
32	KJ193393.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
33	KJ193394.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
34	KJ193396.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
35	KJ193403.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa

36	KJ193395.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
37	KJ193402.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
38	KJ193404.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
39	KJ193400.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
40	KJ193401.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
41	HQ450803.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
42	HQ450804.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
43	HQ450805.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa

44	KJ193526.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
45	KJ193528.1	<i>Manis tricuspis</i>	Tree pangolin	Phylogenetic analysis	Africa
46	KJ193389.1	<i>Manis tetradactyla</i>	Long-tailed pangolin	Phylogenetic analysis	Africa
47	KJ193391.1	<i>Manis tetradactyla</i>	Long-tailed pangolin	Phylogenetic analysis	Africa
48	KJ193392.1	<i>Manis tetradactyla</i>	Long-tailed pangolin	Phylogenetic analysis	Africa
49	KJ193390.1	<i>Manis tetradactyla</i>	Long-tailed pangolin	Phylogenetic analysis	Africa
50	KJ193388.1	<i>Manis tetradactyla</i>	Long-tailed pangolin	Phylogenetic analysis	Africa
51	KP261035.1	<i>Manis temminckii</i>	Ground pangolin	Phylogenetic analysis	Africa

52	KJ193382.1	<i>Manis gigantea</i>	Giant pangolin	Phylogenetic analysis	Africa	
53	KJ193383.1	<i>Manis gigantea</i>	Giant pangolin	Phylogenetic analysis	Africa	
54	KJ193384.1	<i>Manis gigantea</i>	Giant pangolin	Phylogenetic analysis	Africa	
55	KJ193385.1	<i>Manis gigantea</i>	Giant pangolin	Phylogenetic analysis	Africa	
56	KJ193386.1	<i>Manis gigantea</i>	Giant pangolin	Phylogenetic analysis	Africa	
57	NC_001700.1	<i>Felis catus</i>	Cat	Phylogenetic analysis	-	Used as an outgroup
58	NC_002008.4	<i>Canis lupus familiaris</i>	Dog	Phylogenetic analysis	-	Used as an outgroup

Table S2: Summary Stats of scale microbiomes. Sequencing of the microbiomes of three individual pangolin scales (CS1, CS2 and CS3) yielded 12.4 Gbp, 12.2 Gbp and 12.1 Gbp clean data, respectively. The pangolin DNA sequences were discarded and the remaining reads were used for assembly.

Scale Sample	# of Clean Base	Contig Number	Assembly (bp)	Length	N50 (bp)	Max (bp)	Min (bp)	Avg Size (bp)
CS1	12439016760	29400	25077932		835	22906	500	852
CS2	12201424374	128485	150060671		1288	90198	500	1167
CS3	12147247838	35959	34252785		921	62222	500	952

Table S3: List of 61 prominent proteins identified in pangolin scale. Proteins presented in at least 5 out of 6 experimental sets with at least 96% protein sequence identity were selected for downstream analysis.

ID	Protein identification probability	Exclusive unique peptide count	Exclusiv e unique spectrum count	Total spectrum count	Gene Description	Gene Symbol	Molecular Weight	Accession Number
MMP0009559	100.00%	43	45	46	desmoplakin isoform I/desmoplakin	DSP	320 kDa	NP_004406.2
MMP0022578	100.00%	32	50	136	keratin 1	KRT1	63 kDa	AFA52003.1

	100.00%	22	35	86	keratin, type I			
MMP0013009					cytoskeletal 17	KRT17	141 kDa	NP_000413.1
MMP0017553	100.00%	26	31	69	keratin, hair, basic, 4	KRT84	207 kDa	EAW96623.1
MMP0015052	100.00%	11	15	67	keratin, hair, basic, 4	KRT31	133 kDa	NP_002268.2
MMP0017552	100.00%	18	24	61	keratin, type II	KRT85	61 kDa	NP_002274.1
					cuticular Hb5			
					isoform 1			
MMP0022581	100.00%	21	26	59	keratin, type II	KRT5	52 kDa	NP_000415.2
					cytoskeletal 5			
	100.00%	6	7	47	keratin, type II			NP_001307127.
MMP0022062					cuticular Hb6	KRT86	43 kDa	1
MMP0022283	100.00%	24	46	117	keratin, type I	KRT10	49 kDa	NP_000412.3
					cytoskeletal 10			
	100.00%	16	20	35	keratin, type I			
MMP0015051					cuticular Ha6	KRT36	142 kDa	NP_003762.1
	100.00%	5	6	39	keratin, type II			
MMP0022065					cuticular Hb1	KRT81	42 kDa	NP_002272.2

	100.00%	5	5	33	keratin, type II			
MMP0022586					cytoskeletal 79	KRT79	109 kDa	NP_787028.1
MMP0020663	100.00%	8	15	32	protein S100-A9	S100A9	14 kDa	NP_002956.1
MMP0020662	100.00%	6	9	17	protein S100-A12	S100A12	11 kDa	NP_005612.1
	100.00%	10	13	15	heat shock protein			
MMP0007498					beta-1	HSPB1	23 kDa	NP_001531.1
	100.00%	6	9	14	protein S100-A8			NP_001306125.
MMP0020661					isoform a	S100A8	12 kDa	1
	100.00%	10	12	13	leucine-rich repeat-			
					containing protein 15			NP_001128529.
MMP0012274					isoform a precursor	LRRC15	74 kDa	2
	100.00%	8	8	11				NP_001035972.
MMP0021430					galectin-7	LGALS7	15 kDa	1
MMP0017372	100.00%	9	10	10	desmoglein 1	DSG1	104 kDa	AAC83817.1
	100.00%	7	8	10				NP_001339702.
MMP0013018					junction plakoglobin	JUP	92 kDa	1
MMP0006290	100.00%	6	8	10	cystatin-A	CSTA	11 kDa	NP_005204.1

MMP0019755	100.00%	8	9	10	Annexin A2	ANXA2	39 kDa	AAH66955.2
MMP0016378	100.00%	6	6	9	14-3-3 protein sigma	SFN	28 kDa	NP_006133.1
	100.00%	8	8	8	desmocollin-1			
					isoform	Dsc1a		
MMP0010974					preproprotein	DSC1	103 kDa	NP_077739.1
MMP0019685	100.00%	7	8	8	lamin isoform A	LMNA	61 kDa	NP_733821.1
	99.98%	3	3	7				NP_001186883.
MMP0010956					actin, cytoplasmic 2	ACTG1	44 kDa	1
MMP0010355	99.90%	2	2	6	HSPA8 protein	HSPA8	71 kDa	AAH07276.2
MMP0006735	100.00%	5	5	6	delta-globin	HBD	17 kDa	AAL72117.1
	99.98%	4	5	5		HIST2H2B		
MMP0008924					histone H2B type 2-E	E	15 kDa	NP_003519.1
	100.00%	3	4	5	calmodulin-1			NP_001350599.
MMP0010156					isoform 1	CALM3	32 kDa	1
	100.00%	4	5	5	lysozyme	g-like		NP_001358309.
MMP0015108					protein 1 precursor	LYG2	23 kDa	1
MMP0001377	100.00%	4	4	5	thioredoxin	TXN	43 kDa	AAA74596.1

	99.63%	3	4	5	alpha-enolase			
MMP0021817					isoform 1	ENO1	54 kDa	NP_001419.1
	99.38%	4	4	4				
					plakophilin-1			NP_001005337.
MMP0014133					isoform 1a	PKP1	80 kDa	1
	99.38%	4	4	4	elongation factor 1-			
MMP0005472					alpha 1	EEF1A1	50 kDa	NP_001393.1
MMP0008797	99.93%	3	3	4	corneodesmosin	CDSN	46 kDa	CAB57268.1
MMP0001084	99.47%	3	4	4	lysozyme C	LYZ	12 kDa	NP_000230.1
	92.90%	3	3	3	antileukoproteinase			
MMP0018627					precursor	SLPI	14 kDa	NP_003055.1
	99.97%	2	2	3	calmodulin-2			NP_001292554.
MMP0017965					isoform 3	CALM2	12 kDa	1
MMP0009364	99.38%	2	3	3	annexin A1	ANXA1	42 kDa	NP_000691.1
MMP0008849	99.20%	2	2	3	PPIA	PPIA	22 kDa	CAG32988.1
MMP0011249	99.03%	2	3	3	protein S100-P	S100P	14 kDa	NP_005971.1

	99.08%	2	2	2				NP_001029249.
MMP0006894					histone H4	HIST2H4B	11 kDa	1
MMP0002446	99.58%	2	2	2	glyceraldehyde-3-phosphate dehydrogenase	GAPDH	36 kDa	CAA25833.1
	98.30%	1	1	5	keratin, type II			
MMP0017554					cytoskeletal 75	KRT75		NP_004684.2
	98.95%	2	2	2	macrophage migration inhibitory factor			
MMP0020037						MIF	12 kDa	NP_002406.1
MMP0001991	98.48%	1	1	1	KRTAP13-1 protein	KRTAP13-1	16 kDa	AAI13537.1
					G(M2) activator			
MMP0022707	99.08%	6	7	7	protein	GM2A		CAA34215.1
					protein disulfide-isomerase	A6		NP_001269634.
MMP0004767	99.96%	4	6	6	isoform b	PDIA6		1
MMP0012518	97.08%	1	2	4	alpha actinin 4	ACTN4		BAA24447.1

MMP0022782	84.82%	3	3	4	HSPA5 protein methanethiol oxidase	HSPA5	AAI12964.1
MMP0003324	99.76%	3	3	4	isoform 1 tubulin beta chain	SELENBP1	NP_003935.2
MMP0015030	99.68%	3	3	3	isoform b 60S acidic ribosomal	TUBB	NP_821133.1
MMP0023321	98.84%	2	2	3	protein P2 heat shock 70 kDa	RPLP2	NP_000995.1
MMP0014211	83.73%	1	1	3	protein 1A	HSPA1A	NP_005336.3 NP_001291390.
MMP0005114	99.16%	2	2	2	serpin A12 precursor	SERPINA12	1
MMP0018835	99.18%	2	2	2	Nm23 protein lactoperoxidase isoform 1	NME1	CAA35621.1
MMP0005706	99.10%	2	2	2	preproprotein protein S100-A2	LPO	NP_006142.1
MMP0005252	96.13%	1	1	2	isoform 1	S100A2	NP_005969.2

MMP0015049	99.28%	2	2	2	protein S100-A11 V-set and immunoglobulin domain-containing	S100A11	NP_005611.1 NP_001013683.
MMP0016181	98.66%	1	1	1	protein 8	VSIG8	1

Table S4: GO term enrichment analysis of 61 scale proteins.

GO cellular component		Number of Scale Proteins	Expected	Over/under- presentation	Fold Enrichment	FDR	Genes
extracellular (GO:0070062)	exosome	42	6.42	+	6.54	9.51E-24	TUBB, HSPA8, KRT10, KRT36, PDIA6, PPIA, KRT1, KRT75, JUP, NME1, GAPDH, RPLP2, S100A11, ANXA1, HSPA1A, DSC1, KRT84, HSPA5, SFN, DSP, LRRC15, KRT31, ENO1, HSPB1, LGALS7, S100A9, EEF1A1, S100A8, ACTN4, SLPI

cornified (GO:0001533)	envelope	10	0.14	+	72.65	1.35E-13	KRT10, KRT1, JUP, ANXA1, DSC1, DSP, PKP1, CSTA, DSG1, CDSN
keratin (GO:0045095)	filament	11	0.32	+	33.92	6.10E-12	KRT10, KRT36, KRT1, KRT75, KRT86, KRT84, KRT81, KRT5, KRT79, KRT85, KRT17
cytosol (GO:0005829)		42	16.49	+	2.55	1.94E-09	TUBB, LMNA, HSPA8, KRT10, KRT36, PDIA6, PPIA, KRT1, KRT75, JUP, NME1, KRT86, GAPDH, RPLP2, ANXA1, HSPA1A, KRT84, HSPA5, SFN, KRT81, KRTAP13-1, KRT31, ENO1, HSPB1, LGALS7, S100A9, EEF1A1, HBD, S100A8, ACTN4, CSTA, GM2A, ACTG1, KRT5, DSG1, KRT79, S100A12, MIF, KRT85, KRT17, SELENBP1, TXN
desmosome (GO:0030057)		6	0.08	+	75.44	4.35E-08	JUP, DSC1, DSP, PKP1, DSG1, CDSN

focal (GO:0005925)	adhesion	11	1.28	+	8.56	4.50E-06	HSPA8, PPIA, JUP, RPLP2, ANXA1, HSPA1A, HSPA5, HSPB1, SFN, ACTN4, ACTG1
ficolin-1-rich lumen (GO:1904813)	granule	7	0.38	+	18.45	9.15E-06	HSPA1, KRT1, PPIA, JUP, HSPA1A, EEF1A1, MIF
ficolin-1-rich membrane (GO:0101003)	granule	4	0.19	+	21.44	2.40E-03	DSC1, DSP, PKP1, DSG1
sarcomere (GO:0030017)		6	0.64	+	9.34	2.55E-03	JUP, ENO1, HSPB1, CALM3, ACTN4, CALM2
blood (GO:0072562)	microparticle	5	0.44	+	11.35	4.42E-03	HSPA8, KRT1, HSPA1A, HBD, ACTG1
azurophil (GO:0035578)	granule lumen	4	0.28	+	14.53	8.78E-03	TUBB, GM2A, ANXA2, LYZ
adherens (GO:0005912)	junction	5	0.53	+	9.45	9.08E-03	JUP, S100A11, ANXA1, PKP1, ANXA2

collagen-containing extracellular matrix (GO:0062023)	7	1.31	+	5.36	1.40E-02	KRT1, ANXA1, LRRC15, S100A9, S100A8, SLPI, ANXA2
melanosome (GO:0042470)	4	0.34	+	11.89	1.56E-02	HSPA8, PDIA6, HSPA5, ANXA2
fascia adherens (GO:0005916)	2	0.03	+	65.38	2.14E-02	JUP, DSP
nucleus (GO:0005634)	37	23.36	+	1.58	2.15E-02	TUBB, LMNA, HSPA8, KRT10, PPIA, KRT1, JUP, NME1, GAPDH, S100A11, ANXA1, HSPA1A, HSPA5, SFN, DSP, PKP1, ENO1, HSPB1, DSP, LGALS7, S100A9, EEF1A1, SFN, CALM3, S100A8, ACTN4, CSTA, ACTG1, ANXA2, KRT5, CALM2, S100A12, HIST2H4B, S100P, MIF, SELENBP1, TXN

endoplasmic chaperone (GO:0034663)	reticulum complex	2	0.03	+	59.44	2.44E-02	PDIA6, HSPA5
specific (GO:0035580)	granule lumen	3	0.19	+	15.82	3.54E-02	JUP, SLPI, LYZ
lateral plasma (GO:0016328)	membrane	3	0.21	+	14.01	4.72E-02	JUP, ANXA1, DSG1

Table S5: Distribution of 61 scale proteins across exosome-producing cells and tissues. This analysis considered only normal cells and tissues as reported in the ExoCarta database.

Cell Type	Number of Scale Protein	Percentage (%)	Gene Symbol
Mesenchymal stem cells	29	47.5	ACTN4, ANXA1, ANXA2, DSP, EEF1A1, ENO1, GAPDH, HIST2H2BE, HIST2H4B, HSPA1A, HSPA5, HSPB1, JUP, KRT1, KRT10, KRT17, KRT5, KRT79, KRT84, LMNA, LYZ, MIF, NME1, PPIA, S100A11, S100A8, S100P, SFN, TUBB
Platelets	26	42.6	ACTG1, ACTN4, ANXA1, ANXA2, CDSN, CSTA, DSC1, DSG1, DSP, EEF1A1, ENO1,

			GAPDH, HBD, HSPA1A, HSPA5, HSPB1, JUP, LGALS7, LYZ, NME1, PDIA6, PPIA, S100A8, S100A9, SFN, TUBB
Thymus	21	34.4	ANXA1, ANXA2, CALM2, CALM3, DSP, EEF1A1, ENO1, HIST2H4B, HSPA1A, HSPA5, HSPB1, JUP, LGALS7, NME1, PDIA6, PPIA, RPLP2, S100A11, SFN, TUBB, TXN
Keratinocytes	17	27.9	SFN, ACTG1, ACTN4, ANXA1, ANXA2, EEF1A1, ENO1, GAPDH, GM2A, HIST2H4B, HSPA1A, HSPB1, KRT1, KRT10, KRT5, LGALS7, PPIA
B cells	15	24.6	EEF1A1, ENO1, GAPDH, TUBB, ACTN4, ANXA2, CALM2, DSP, HSPA1A, HSPA5, MIF, PDIA6, PPIA, RPLP2, TXN
Tracheobronchial cells	8	13.1	ANXA1, ANXA2, CALM2, CALM3, GAPDH, HSPA1A, MIF, PPIA
Intestinal epithelial cells	4	6.6	ENO1, GAPDH, KRT1, KRT10
Aqueous humor	3	4.9	ANXA1, ANXA2, GAPDH
Tabecular meshwork cells	3	4.9	ANXA1, ANXA2, GAPDH
Endothelial cells	2	3.3	HIST2H2BE, HSPA5

Amniotic fluid	1	1.6	ANXA1
Plasma	1	1.6	HBD

Table S6: STRING-annotated 61 proteins identified in pangolin scale. Significant enriched biological processes (FDR<0.05) associated with the scale proteins were predicted by STRING.

ID	Gene Description	Gene Symbol	STRING Protein Interacting Network	Significant Enriched Biological Process (STRING)
MMP0010956	actin, cytoplasmic 2	ACTG1	Immune Response Network, Stress Response Network	defense response, secretion by cell, cellular response to chemical stimulus
MMP0009364	annexin A1	ANXA1	Immune Response Network, Stress Response Network	defense response, regulation of peptide transport, secretion by cell, response to external stimulus, cellular response to chemical stimulus
MMP0019755	Annexin A2	ANXA2	Immune Response Network	defense response
MMP0010974	desmocollin-1 isoform Dsc1a preproprotein	DSC1	Immune Response Network, Keratinization Network	neutrophil degranulation, cornification, cell-cell adhesion
MMP0017372	desmoglein 1	DSG1	Immune Response Network, Keratinization Network	neutrophil degranulation, cornification, cell-cell adhesion, cell junction assembly
MMP0009559	desmoplakin isoform I/desmoplakin	DSP	Immune Response Network, Keratinization Network, Stress Response Network	neutrophil degranulation, cornification, cell-cell adhesion, peptide cross-linking, intermediate

					filament organization, desmosome organization, secretion by cell
MMP0005472	elongation factor 1- alpha 1	EEF1A1	Immune Response Network		neutrophil degranulation
MMP0002446	glyceraldehyde-3- phosphate dehydrogenase	GAPDH	Immune Response Network, Stress Response Network		antimicrobial humoral response, defense response, peptidyl-cysteine S-nitrosylation, regulation of peptide transport, defense response to other organism, response to external stimulus, cellular response to chemical stimulus
MMP0022707	G(M2) protein	activator GM2A	Immune Response Network		neutrophil degranulation
MMP0008924	histone H2B type 2-E	HIST2H2BE	Immune Response Network, Stress Response Network		antimicrobial humoral response, defense response, response to external stimulus, defense response to other organism
MMP0014211	heat shock 70 kDa protein 1A	HSPA1A	Immune Response Network, Stress Response Network		neutrophil degranulation, secretion by cell, response to unfolded protein, cellular response to chemical stimulus

MMP0010355	HSPA8 protein	HSPA8	Immune Response Network, Stress Response Network	neutrophil degranulation, regulation of peptide transport
MMP0013018	junction plakoglobin	JUP	Immune Response Network, Keratinization Network	neutrophil degranulation, regulation of peptide transport, cornification, cell-cell adhesion, cell junction assembly, desmosome organization
MMP0022578	keratin 1	KRT1	Immune Response Network, Keratinization Network, Stress Response Network	neutrophil degranulation, defense response, cornification, peptide cross-linking, secretion by cell
MMP0001084	lysozyme C	LYZ	Immune Response Network, Stress Response Network	neutrophil degranulation, defense response, antimicrobial humoral response, response to external stimulus, defense response to other organism, secretion by cell
MMP0020037	macrophage migration inhibitory factor	MIF	Immune Response Network	neutrophil degranulation, regulation of peptide transport, defense response
MMP0014133	plakophilin-1 isoform 1a	PKP1	Immune Response Network, Keratinization Network	neutrophil degranulation, cornification, cell-cell adhesion, intermediate filament organization

MMP0008849	PPIA	PPIA	Immune Response Network	neutrophil degranulation, regulation of peptide transport
MMP0015049	protein S100-A11	S100A11	Immune Response Network	neutrophil degranulation
MMP0020662	protein S100-A12	S100A12	Immune Response Network, Stress Response Network	antimicrobial humoral response, defense response, neutrophil degranulation, defense response to other organism, secretion by cell, response to external stimulus, cellular response to chemical stimulus
MMP0020661	protein isoform a	S100-A8 S100A8	Immune Response Network, Stress Response Network	antimicrobial humoral response, defense response, neutrophil degranulation, peptidyl-cysteine S-nitrosylation, regulation of peptide transport, defense response to other organism, secretion by cell, response to external stimulus, cellular response to chemical stimulus

MMP0020663	protein S100-A9	S100A9	Immune Response Network, Stress Response Network	antimicrobial humoral response, defense response, neutrophil degranulation, peptidyl-cysteine S-nitrosylation, regulation of peptide transport, defense response to other organism, secretion by cell, response to external stimulus, cellular response to chemical stimulus
MMP0011249	protein S100-P	S100P	Immune Response Network	neutrophil degranulation
MMP0018627	antileukoproteinase precursor	SLPI	Immune Response Network, Stress Response Network	antimicrobial humoral response, defense response, neutrophil degranulation
MMP0015030	tubulin beta chain isoform b	TUBB	Immune Response Network, Stress Response Network	neutrophil degranulation, defense response, secretion by cell
MMP0008797	corneodesmosin	CDSN	Keratinization Network	cornification, cell-cell adhesion
MMP0006290	cystatin-A	CSTA	Keratinization Network	cornification, cell-cell adhesion, peptide cross-linking
MMP0022283	keratin, type I cytoskeletal 10	KRT10	Keratinization Network	cornification, peptide cross-linking

MMP0015051	keratin, type I cuticular Ha6	KRT36	Keratinization Network	cornification
MMP0022581	keratin, type II cytoskeletal 5	KRT5	Keratinization Network	cornification, cell junction assembly
MMP0017554	keratin, type II cytoskeletal 75	KRT75	Keratinization Network	cornification
MMP0022586	keratin, type II cytoskeletal 79	KRT79	Keratinization Network	cornification
MMP0022065	keratin, type II cuticular Hb1	KRT81	Keratinization Network	cornification
MMP0017553	keratin, hair, basic, 4	KRT84	Keratinization Network	cornification
MMP0017552	keratin, type II cuticular Hb5 isoform 1	KRT85	Keratinization Network	cornification
MMP0022062	keratin, type II cuticular Hb6	KRT86	Keratinization Network	cornification
MMP0001991	KRTAP13-1 protein	KRTAP13-1	Keratinization Network	cornification

MMP0016378	14-3-3 protein sigma	SFN	Keratinization Network, Stress Response Network	
MMP0012518	alpha actinin 4	ACTN4	Stress Response Network	secretion by cell
MMP0006735	delta-globin	HBD	Stress Response Network	
MMP0006894	histone H4	HIST2H4B	Stress Response Network	
MMP0022782	HSPA5 protein	HSPA5	Stress Response Network	response to external stimulus, response to unfolded protein, cellular response to chemical stimulus
MMP0007498	heat shock protein beta-1	HSPB1	Stress Response Network	response to external stimulus, response to unfolded protein, cellular response to chemical stimulus
MMP0019685	lamin isoform A	LMNA	Stress Response Network	cellular response to chemical stimulus, response to unfolded protein
MMP0005706	lactoperoxidase isoform 1 preproprotein	LPO	Stress Response Network	defense response to other organism, response to external stimulus, cellular response to chemical stimulus

MMP0015108	lysozyme	g-like	LYG2	Stress Response Network	response to external stimulus, defense response to other organism
	protein 1 precursor				
MMP0004767	protein	disulfide-	PDIA6	Stress Response Network	cellular response to chemical stimulus, response to unfolded protein
	isomerase A6 isoform				
	b				
MMP0013009	keratin,	type	I	Keratinization Network	cornification, intermediate filament organization
	cytoskeletal 17				
MMP0015052	keratin, hair, basic, 4		KRT31	Keratinization Network	cornification
MMP0017965	calmodulin-2	isoform	CALM2		
	3				
MMP0010156	calmodulin-1	isoform	CALM3		
	1				
MMP0021817	alpha-enolase	isoform	ENO1		
	1				
MMP0021430	galectin-7		LGALS7		

MMP0012274	leucine-rich repeat- containing protein 15 isoform a precursor	LRRC15
MMP0018835	Nm23 protein	NME1
MMP0023321	60S acidic ribosomal protein P2	RPLP2
MMP0005252	protein S100-A2 isoform 1	S100A2
MMP0003324	methanethiol oxidase isoform 1	SELENBP1
MMP0005114	serpin A12 precursor	SERPINA12
MMP0001377	thioredoxin	TXN
MMP0016181	V-set and immunoglobulin domain-containing protein 8	VSIG8

Table S7: List of 94 prominent proteins identified in pangolin scale. Proteins presented in at least 3 out of 6 experimental sets with at least 96% protein sequence identity were selected for downstream analysis.

ID	Protein Identification Probability	Exclusive Unique Peptide Count	Exclusive Unique Spectrum Count	Total Spectrum Count	Gene Description	Gene Symbol
MMP0009559	100.00%	43	45	46	desmoplakin isoform I/desmoplakin	DSP
MMP0022578	100.00%	32	50	136	keratin 1	KRT1
MMP0013009	100.00%	22	35	86	keratin, type I cytoskeletal 17	KRT17
MMP0017553	100.00%	26	31	69	keratin, hair, basic, 4	KRT84
MMP0015052	100.00%	11	15	67	keratin, hair, basic, 4	KRT31
MMP0017552	100.00%	18	24	61	keratin, type II cuticular Hb5 isoform 1	KRT85
MMP0022581	100.00%	21	26	59	keratin, type II cytoskeletal 5	KRT5
MMP0022062	100.00%	6	7	47	keratin, type II cuticular Hb6	KRT86
MMP0022283	100.00%	24	46	117	keratin, type I cytoskeletal 10	KRT10
MMP0015051	100.00%	16	20	35	keratin, type I cuticular Ha6	KRT36
MMP0022065	100.00%	5	6	39	keratin, type II cuticular Hb1	KRT81

MMP0022586	100.00%	5	5	33	keratin, type II cytoskeletal 79	KRT79
MMP0020663	100.00%	8	15	32	protein S100-A9	S100A9
MMP0020662	100.00%	6	9	17	protein S100-A12	S100A12
MMP0007498	100.00%	10	13	15	heat shock protein beta-1	HSPB1
MMP0020661	100.00%	6	9	14	protein S100-A8 isoform a	S100A8
MMP0012274	100.00%	10	12	13	leucine-rich repeat-containing protein 15 isoform a precursor	LRRC15
MMP0021430	100.00%	8	8	11	galectin-7	LGALS7
MMP0017372	100.00%	9	10	10	desmoglein 1	DSG1
MMP0013018	100.00%	7	8	10	junction plakoglobin	JUP
MMP0006290	100.00%	6	8	10	cystatin-A	CSTA
MMP0019755	100.00%	8	9	10	Annexin A2	ANXA2
MMP0016378	100.00%	6	6	9	14-3-3 protein sigma	SFN
MMP0010974	100.00%	8	8	8	desmocollin-1 isoform Dsc1a preproprotein	DSC1
MMP0019685	100.00%	7	8	8	lamin isoform A	LMNA
MMP0010956	99.98%	3	3	7	actin, cytoplasmic 2	ACTG1

MMP0010355	99.90%	2	2	6	HSPA8 protein	HSPA8
MMP0006735	100.00%	5	5	6	delta-globin	HBD
MMP0008924	99.98%	4	5	5	histone H2B type 2-E	HIST2H2BE
MMP0010156	100.00%	3	4	5	calmodulin-1 isoform 1	CALM3
MMP0015108	100.00%	4	5	5	lysozyme g-like protein 1 precursor	LYG2
MMP0001377	100.00%	4	4	5	thioredoxin	TXN
MMP0021817	99.63%	3	4	5	alpha-enolase isoform 1	ENO1
MMP0014133	99.38%	4	4	4	plakophilin-1 isoform 1a	PKP1
MMP0005472	99.38%	4	4	4	elongation factor 1-alpha 1	EEF1A1
MMP0008797	99.93%	3	3	4	corneodesmosin	CDSN
MMP0001084	99.47%	3	4	4	lysozyme C	LYZ
MMP0018627	92.90%	3	3	3	antileukoproteinase precursor	SLPI
MMP0017965	99.97%	2	2	3	calmodulin-2 isoform 3	CALM2
MMP0009364	99.38%	2	3	3	annexin A1	ANXA1
MMP0008849	99.20%	2	2	3	PPIA	PPIA
MMP0011249	99.03%	2	3	3	protein S100-P	S100P
MMP0006894	99.08%	2	2	2	histone H4	HIST2H4B

MMP0002446	99.58%	2	2	2	glyceraldehyde-3-phosphate dehydrogenase	GAPDH
MMP0017554	98.30%	1	1	5	keratin, type II cytoskeletal 75	KRT75
MMP0020037	98.95%	2	2	2	macrophage migration inhibitory factor	MIF
MMP0001991	98.48%	1	1	1	KRTAP13-1 protein	KRTAP13-1
MMP0022707	99.08%	6	7	7	G(M2) activator protein	GM2A
MMP0004767	99.96%	4	6	6	protein disulfide-isomerase A6 isoform b	PDIA6
MMP0012518	97.08%	1	2	4	alpha actinin 4	ACTN4
MMP0022782	84.82%	3	3	4	HSPA5 protein	HSPA5
MMP0003324	99.76%	3	3	4	methanethiol oxidase isoform 1	SELENBP1
MMP0015030	99.68%	3	3	3	tubulin beta chain isoform b	TUBB
MMP0023321	98.84%	2	2	3	60S acidic ribosomal protein P2	RPLP2
MMP0014211	83.73%	1	1	3	heat shock 70 kDa protein 1A	HSPA1A
MMP0005114	99.16%	2	2	2	serpin A12 precursor	SERPINA12
MMP0018835	99.18%	2	2	2	Nm23 protein	NME1
MMP0005706	99.10%	2	2	2	lactoperoxidase isoform 1 preproprotein	LPO
MMP0005252	96.13%	1	1	2	protein S100-A2 isoform 1	S100A2

MMP0015049	99.28%	2	2	2	protein S100-A11	S100A11
MMP0016181	98.66%	1	1	1	V-set and immunoglobulin domain-containing protein 8	VSIG8
MMP0022067	99.73%	1	2	19	Keratin 83	KRT83
MMP0022587	73.62%	1	1	22	Keratin 76	KRT76
MMP0014482	100.00%	3	4	51	Keratin 33A	KRT33A
MMP0008639	53.92%	1	1	4	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide	YWHAE
MMP0001194	98.92%	1	3	5	calmodulin-like 3	CALML3
MMP0018534	100.00%	2	2	2	protease, serine, 58	PRSS58
MMP0009198	74.43%	1	2	4	syntaxin 3	STX3
MMP0019248	96.53%	5	5	5	chitinase 1 (chitotriosidase)	CHIT1
MMP0002428	90.63%	3	3	4	caspase 14, apoptosis-related cysteine peptidase	CASP14
MMP0019679	93.57%	3	4	4	hornerin	HRNR
MMP0008053	84.17%	2	3	4	galectin 3	LGALS3

MMP0003621	91.30%	2	2	2	serpin peptidase inhibitor, clade B (ovalbumin)	SERPINB5
MMP0000829	90.66%	2	2	2	suprabasin	SBSN
MMP0010973	89.67%	4	4	4	desmocollin 3	DSC3
MMP0022284	92.58%	2	2	3	Keratin 23	KRT23
MMP0022614	77.00%	2	2	2	D-dopachrome tautomerase-like	DDTL
MMP0008927	93.00%	1	1	2	histone cluster 2, H2aa4	H2AC19
MMP0004845	77.60%	2	2	2	keratin associated protein 8-1	KRTAP8-1
MMP0013439	99.37%	3	3	3	gamma-glutamyl hydrolase (conjugase, folylpolygammaglutamyl hydrolase)	GGH
MMP0000322	93.34%	2	2	2	peroxiredoxin 6	PRDX6
MMP0021423	84.70%	3	3	3	nucleolin	NCL
MMP0020799	99.35%	2	2	2	capping protein (actin filament), gelsolin-like	CAPG
MMP0022673	99.08%	2	2	2	capping protein (actin filament), gelsolin-like	HAL

MMP0000462	91.48%	2	2	2	histidine ammonia-lyase	LDHA
MMP0014455	100.00%	2	3	29	triosephosphate isomerase 1	TPI1
MMP0021381	99.05%	2	2	2	extracellular matrix protein 1	ECM1
MMP0000979	97.78%	2	2	2	creatine kinase, brain	CKB
MMP0018355	99.30%	2	2	2	tubulin, alpha 1c	TUBA1C
MMP0005486	99.33%	2	2	2	tubulin, alpha 4a	TUBA4A
MMP0010666	99.20%	2	2	2	heavy chain 9, non-muscle	MYH9
MMP0003933	98.65%	1	1	1	N-acylsphingosine amidohydrolase (acid ceramidase) 1	ASAH1
MMP0021328	98.90%	1	1	1	cysteine conjugate-beta lyase 2	KYAT3
MMP0007759	97.47%	1	1	1	diazepam binding inhibitor (GABA DBI receptor modulator, acyl-CoA binding protein)	

Notes:

Protein Identification Probability=Scaffold's calculated probability that the protein identification for any of the MS Samples is correct.

Exclusive Unique Peptide Count= The number of different amino acid sequences, regardless of any modification that are associated with a single protein group.

Exclusive Unique Spectrum Count=Number of distinct spectra associated only with a single protein group.

Total Spectrum Count=The total number of spectra associated to a single protein group, including those shared with other proteins.

Table S8: Gene Ontology Biological Process enrichment analysis of 94 scale proteins using STRING database.

GO Term ID	Term description	Observed gene count	Background gene count	Strength	False discovery rate	Matching proteins in your network
GO:0030216	Keratinocyte differentiation	20	138	1.48	3.32E-19	KRT5, KRT1, KRT75, KRT85, KRT84, CSTA, KRT10, KRT83, KRT17, KRT79, KRT76, SFN, HRNR, CDSN, ANXA1, DSP, KRT81, ASAH1, CASP14, KRT86
GO:0045109	Intermediate filament organization	17	69	1.71	3.32E-19	KRT33A, KRT23, KRT31, KRT5, KRT1, KRT75, KRT85, KRT84, PKP1, KRT83, KRT17, KRT79, KRT36, KRT76, DSP, KRT81, KRT86
GO:0043588	Skin development	21	266	1.22	5.66E-16	KRT5, KRT1, KRT75, KRT85, KRT84, CSTA, KRT10, KRT83, KRT17, KRT79, KRT76, SFN, HRNR, CDSN, ANXA1, DSP, KRT81, ASAH1, JUP, CASP14, KRT86
GO:0008544	Epidermis development	21	320	1.14	1.69E-14	KRT31, KRT5, KRT1, KRT75, KRT85, KRT84, CSTA, KRT10, KRT83, KRT17, KRT79, KRT76, SFN, HRNR, CDSN, ANXA1, DSP, KRT81, ASAH1, CASP14, KRT86
GO:0030855	Epithelial cell differentiation	26	617	0.95	3.28E-14	KRT33A, KRT23, KRT31, KRT5, KRT1, KRT75, LGALS3, KRT85, KRT84, CSTA, KRT10, KRT83, KRT17, KRT79, KRT36, KRT76, TUBB, SFN, HRNR, CDSN, ANXA1, DSP, KRT81, ASAH1, CASP14, KRT86

GO:0031424	Keratinization	14	83	1.55	3.84E-14	KRT5, KRT1, KRT75, KRT85, KRT84, KRT83, KRT17, KRT79, KRT76, SFN, HRNR, KRT81, CASP14, KRT86
GO:0060429	Epithelium development	28	1069	0.74	1.43E-10	KRT33A, KRT23, KRT31, KRT5, KRT1, KRT75, LGALS3, KRT85, KRT84, CSTA, KRT10, KRT83, KRT17, KRT79, KRT36, KRT76, TUBB, SFN, HRNR, CDSN, ANXA1, DSP, KRT81, ASAH1, SERPINB5, CASP14, KRT86, ACTG1
GO:0097435	Supramolecular fiber organization	20	570	0.87	5.50E-09	KRT33A, KRT23, KRT31, KRT5, KRT1, KRT75, KRT85, KRT84, CAPG, PKP1, KRT83, KRT17, KRT79, KRT36, KRT76, ANXA2, DSP, KRT81, KRT86, ACTG1
GO:0007010	Cytoskeleton organization	27	1229	0.66	2.04E-08	KRT33A, KRT23, MYH9, TUBA4A, KRT31, KRT5, KRT1, KRT75, ACTN4, KRT85, KRT84, CAPG, PKP1, KRT83, KRT17, KRT79, KRT36, KRT76, TUBB, LMNA, ANXA1, DSP, KRT81, GAPDH, TUBA1C, KRT86, ACTG1
GO:0098609	Cell-cell adhesion	18	542	0.84	1.52E-07	MYH9, HSPB1, DSG1, DSC1, PKP1, CSTA, S100A11, ANXA2, DSC3, S100A8, S100A9, CDSN, ANXA1, LGALS7, DSP, JUP, PPIA, ACTG1
GO:0009888	Tissue development	30	1723	0.56	2.71E-07	KRT33A, KRT23, KRT31, KRT5, KRT1, KRT75, LGALS3, KRT85, KRT84, CSTA, KRT10, KRT83, KRT17, KRT79, KRT36, KRT76, TUBB, SFN, LMNA, HRNR, ECM1, CDSN, ANXA1, DSP, KRT81, ASAH1, SERPINB5, CASP14, KRT86, ACTG1
GO:0030154	Cell differentiation	39	3507	0.37	8.29E-05	KRT33A, KRT23, MYH9, KRT31, KRT5, KRT1, KRT75, ACTN4, LGALS3, KRT85, KRT84, YWHAE, CSTA, KRT10, KRT83, KRT17, HSPA5, KRT79, KRT36, KRT76, NME1, STX3, TUBB, SFN, ANXA2, LMNA, S100A8, S100A9, HRNR, ECM1, CDSN, ANXA1, DSP, KRT81, ASAH1,

GO:0021762	Substantia nigra development	6	47	1.43	0.00017	CASP14, PPIA, KRT86, ACTG1 YWHAE, CALM3, CKB, HSPA5, LDHA, CALM2
GO:0048856	Anatomical structure development	48	5117	0.29	0.00017	KRT33A, KRT23, MYH9, KRT31, KRT5, KRT1, KRT75, ACTN4, LGALS3, KRT85, KRT84, CAPG, YWHAE, CSTA, KRT10, CALM3, KRT83, CKB, KRT17, NCL, HSPA5, KRT79, KRT36, KRT76, NME1, STX3, TUBB, SFN, ANXA2, DSC3, LMNA, S100A8, S100A9, HRNR, ECM1, CDSN, ANXA1, DSP, KRT81, ASAH1, SERPINB5, JUP, CASP14, PPIA, KRT86, LDHA, ACTG1, CALM2
GO:0034109	Homotypic cell-cell adhesion	6	60	1.32	0.00058	MYH9, HSPB1, DSP, JUP, PPIA, ACTG1
GO:0018149	Peptide cross-linking	5	37	1.45	0.0011	KRT1, CSTA, KRT10, ANXA1, DSP
GO:0006996	Organelle organization	36	3470	0.34	0.0012	KRT33A, KRT23, MYH9, H4C6, TUBA4A, KRT31, KRT5, KRT1, KRT75, ACTN4, KRT85, KRT84, CAPG, PKP1, CALM3, KRT83, KRT17, KRT79, KRT36, KRT76, STX3, TUBB, SFN, ANXA2, LMNA, H2BC21, HSPA1A, ANXA1, DSP, KRT81, GAPDH, PPIA, TUBA1C, KRT86, ACTG1, CALM2
GO:0044419	Biological process involved in interspecies interaction between organisms	22	1490	0.49	0.0012	MIF, HSPB1, KRT1, LGALS3, LYZ, LPO, LYG2, TUBB, SLPI, CHIT1, S100A8, S100A12, S100A9, H2BC21, HSPA1A, ANXA1, GAPDH, LRRC15, PPIA, HSPA8, ACTG1, ENO1

GO:0051248	Negative regulation of protein metabolic process	18	1038	0.56	0.0013	MIF, HSPB1, LGALS3, YWHAE, CSTA, CALM3, NCL, SFN, SLPI, SERPINA12, ANXA2, ECM1, HSPA1A, SERPINB5, GAPDH, PPIA, DBI, CALM2
GO:1905913	Negative regulation of calcium ion export across plasma membrane	3	4	2.2	0.0022	YWHAE, CALM3, CALM2
GO:0071621	Granulocyte chemotaxis	6	86	1.16	0.0027	LGALS3, S100A8, S100A12, S100A9, ANXA1, PPIA
GO:0018119	Peptidyl-cysteine S-nitrosylation	3	6	2.02	0.0043	S100A8, S100A9, GAPDH
GO:0051346	Negative regulation of hydrolase activity	10	354	0.77	0.0043	LGALS3, CSTA, SFN, SLPI, SERPINA12, ANXA2, ECM1, ANXA1, SERPINB5, GAPDH
GO:0019730	Antimicrobial humoral response	7	149	0.99	0.0044	LGALS3, LYZ, SLPI, S100A12, S100A9, H2BC21, GAPDH
GO:0048513	Animal organ development	33	3246	0.33	0.0044	MYH9, KRT5, KRT1, KRT75, KRT85, KRT84, YWHAE, CSTA, KRT10, CALM3, KRT83, CKB, KRT17, HSPA5, KRT79, KRT76, NME1, SFN, ANXA2, LMNA, HRNR, ECM1, CDSN, ANXA1, DSP, KRT81, ASAH1, SERPINB5, JUP, CASP14, KRT86, LDHA, CALM2
GO:0042026	Protein refolding	4	25	1.53	0.0045	HSPB1, HSPA5, HSPA1A, HSPA8
GO:0006165	Nucleoside diphosphate	5	63	1.22	0.0074	TPI1, NME1, GAPDH, LDHA, ENO1

GO:2001242	phosphorylation Regulation of intrinsic apoptotic signaling pathway	7	169	0.94	0.0083	MIF, HSPB1, S100A8, S100A9, HSPA1A, PPIA, ENO1
GO:0016052	Carbohydrate catabolic process	6	113	1.05	0.0084	TPI1, GM2A, CHIT1, GAPDH, LDHA, ENO1
GO:0009607	Response to biotic stimulus	19	1375	0.46	0.0094	MIF, HSPB1, KRT1, LGALS3, LYZ, LPO, HSPA5, LYG2, TUBB, SLPI, CHIT1, S100A8, S100A12, S100A9, H2BC21, ANXA1, GAPDH, ACTG1, ENO1
GO:0051246	Regulation of protein metabolic process	28	2622	0.35	0.0094	MIF, MYH9, HSPB1, LGALS3, YWHAE, CSTA, CALM3, KRT17, NCL, HSPA5, EEF1A1, SFN, SLPI, SERPINA12, ANXA2, LMNA, S100A8, S100A12, S100A9, ECM1, TXN, HSPA1A, SERPINB5, GAPDH, PPIA, DBI, ENO1, CALM2
GO:0010466	Negative regulation of peptidase activity	8	249	0.83	0.011	CSTA, SFN, SLPI, SERPINA12, ANXA2, ECM1, SERPINB5, GAPDH
GO:0009205	Purine ribonucleoside triphosphate metabolic process	7	188	0.89	0.014	TPI1, NME1, HSPA1A, GAPDH, HSPA8, LDHA, ENO1
GO:0006959	Humoral immune response	8	268	0.8	0.0168	KRT1, LGALS3, LYZ, SLPI, S100A12, S100A9, H2BC21, GAPDH
GO:0030593	Neutrophil chemotaxis	5	80	1.12	0.0169	LGALS3, S100A8, S100A12, S100A9, PPIA
GO:0030162	Regulation of proteolysis	13	739	0.57	0.0171	MYH9, CSTA, SFN, SLPI, SERPINA12, ANXA2, S100A8, S100A9, ECM1, HSPA1A, SERPINB5, GAPDH, ENO1

GO:0051707	Response to other organism	18	1328	0.45	0.0171	MIF, HSPB1, KRT1, LGALS3, LYZ, LPO, LYG2, TUBB, SLPI, CHIT1, S100A8, S100A12, S100A9, H2BC21, ANXA1, GAPDH, ACTG1, ENO1
GO:0033120	Positive regulation of RNA splicing	4	41	1.31	0.0181	NCL, PRDX6, HSPA1A, HSPA8
GO:0052547	Regulation of peptidase activity	10	446	0.67	0.0181	CSTA, SFN, SLPI, SERPINA12, ANXA2, S100A8, S100A9, ECM1, SERPINB5, GAPDH
GO:0070527	Platelet aggregation	4	43	1.29	0.0202	MYH9, HSPB1, PPIA, ACTG1
GO:0098542	Defense response to other organism	15	989	0.5	0.0202	MIF, KRT1, LGALS3, LYZ, LPO, LYG2, TUBB, SLPI, S100A8, S100A12, S100A9, H2BC21, ANXA1, GAPDH, ACTG1
GO:2001233	Regulation of apoptotic signaling pathway	9	365	0.71	0.0202	MIF, HSPB1, LGALS3, LMNA, S100A8, S100A9, HSPA1A, PPIA, ENO1
GO:0050878	Regulation of body fluid levels	9	371	0.71	0.0217	MYH9, HSPB1, KRT1, NME1, SFN, ANXA2, HRNR, PPIA, ACTG1
GO:0006096	Glycolytic process	4	46	1.26	0.0239	TPI1, GAPDH, LDHA, ENO1
GO:0051336	Regulation of hydrolase activity	15	1011	0.49	0.0239	LGALS3, CSTA, CALM3, SFN, SLPI, SERPINA12, ANXA2, S100A8, S100A9, ECM1, HSPA1A, ANXA1, SERPINB5, GAPDH, CALM2
GO:0098869	Cellular oxidant detoxification	5	91	1.06	0.0239	LPO, PRDX6, S100A9, TXN, HBD
GO:0035304	Regulation of	5	93	1.05	0.0243	LGALS3, YWHAE, CALM3, PPIA, CALM2

	protein dephosphorylation					
GO:0010628	Positive regulation of gene expression	16	1146	0.47	0.0249	MIF, MYH9, HSPB1, PKP1, KRT17, NCL, PRDX6, ANXA2, LMNA, HSPA1A, ANXA1, LGALS7, GAPDH, HSPA8, ACTG1, ENO1
GO:0042742	Defense response to bacterium	8	306	0.74	0.028	LYZ, LPO, LYG2, SLPI, S100A8, S100A12, S100A9, H2BC21
GO:0051651	Maintenance of location in cell	5	97	1.03	0.028	HSPA5, GM2A, S100A8, S100A9, TXN
GO:0016043	Cellular component organization	43	5436	0.22	0.029	KRT33A, KRT23, MIF, MYH9, H4C6, TUBA4A, KRT31, KRT5, KRT1, KRT75, ACTN4, DSG1, KRT85, KRT84, CAPG, PKP1, KRT10, CALM3, KRT83, KRT17, KRT79, KRT36, KRT76, STX3, TUBB, SFN, ANXA2, LMNA, HRNR, H2BC21, HSPA1A, ANXA1, DSP, KRT81, SERPINB5, JUP, GAPDH, PPIA, HSPA8, TUBA1C, KRT86, ACTG1, CALM2
GO:0035606	Peptidyl-cysteine S-trans-nitrosylation	2	2	2.32	0.029	S100A9, GAPDH
GO:0070488	Neutrophil aggregation	2	2	2.32	0.029	S100A8, S100A9
GO:2001234	Negative regulation of apoptotic signaling pathway	7	230	0.8	0.029	MIF, HSPB1, LGALS3, LMNA, HSPA1A, PPIA, ENO1
GO:2001243	Negative regulation of	5	101	1.02	0.0311	MIF, HSPB1, HSPA1A, PPIA, ENO1

	intrinsic apoptotic signaling pathway					
GO:0046034	ATP metabolic process	6	163	0.89	0.0316	TPI1, HSPA1A, GAPDH, HSPA8, LDHA, ENO1
GO:0010605	Negative regulation of macromolecule metabolic process	27	2760	0.31	0.0338	MIF, HSPB1, LGALS3, PKP1, YWHAE, CSTA, S100A11, CALM3, NCL, SFN, SLPI, SERPINA12, ANXA2, LMNA, ECM1, TXN, HSPA1A, ANXA1, LGALS7, ASAH1, SERPINB5, GAPDH, PPIA, HSPA8, DBI, ENO1, CALM2
GO:0002027	Regulation of heart rate	5	104	1	0.0341	YWHAE, CALM3, DSP, JUP, CALM2
GO:0010951	Negative regulation of endopeptidase activity	7	240	0.79	0.0345	CSTA, SFN, SLPI, SERPINA12, ANXA2, SERPINB5, GAPDH
GO:0052548	Regulation of endopeptidase activity	9	414	0.66	0.035	CSTA, SFN, SLPI, SERPINA12, ANXA2, S100A8, S100A9, SERPINB5, GAPDH
GO:0043388	Positive regulation of DNA binding	4	58	1.16	0.0402	CALM3, NME1, TXN, CALM2
GO:0050900	Leukocyte migration	7	249	0.77	0.0405	MYH9, LGALS3, S100A8, S100A12, S100A9, ANXA1, PPIA
GO:0061844	Antimicrobial humoral immune response mediated by antimicrobial	5	113	0.97	0.0451	LGALS3, S100A12, S100A9, H2BC21, GAPDH

GO:0050790	peptide Regulation of catalytic activity	24	2370	0.33	0.0461	MIF, HSPB1, LGALS3, CSTA, CALM3, CALML3, EEF1A1, SFN, SLPI, SERPINA12, ANXA2, GM2A, S100A8, S100A12, S100A9, ECM1, TXN, HSPA1A, ANXA1, SERPINB5, GAPDH, PPIA, DBI, CALM2
GO:0045087	Innate immune response	12	754	0.52	0.0469	MIF, KRT1, LGALS3, TUBB, SLPI, S100A8, S100A12, S100A9, H2BC21, ANXA1, GAPDH, ACTG1
GO:0050832	Defense response to fungus	4	62	1.13	0.0473	S100A8, S100A12, S100A9, GAPDH

Table S9: Distribution of 94 scale proteins across exosome-producing cells and tissues. This analysis considered only normal cells and tissues as reported in the ExoCarta database.

Cell Type	Number of Scale Protein	Percentage (%)	Gene Symbol
Mesenchymal stem cells	39	41.5	TUBA1C, TUBB, YWHAE, ACTN4, ANXA1, ANXA2, DSP, ENO1, GAPDH, HSPA1A, MYH9, GAPDH, ENO1, HSPB1, KRT17, LDHA, PPIA, PRDX6, ACTG1, ACTN4, ANXA2, CALM2, CALM3, CKB, DSC1, DSP, EEF1A1, ENO1, GAPDH, HIST2H2BE, HIST2H4B, HSPA1A, HSPA5, HSPB1, JUP, KRT1, KRT10, KRT17, KRT5
Platelets	36	38.3	ANXA1, ACTG1, ACTN4, ENO1, GAPDH, HSPB1, KRT1, LDHA, ANXA2,

			ANXA1, EEF1A1, HIST2H2BE, HIST2H4B, MYH9, NME1, TUBA1C, TUBB, YWHAE, CKB, MIF, S100A11, RPLP2, HSPA1A, KRT5, KRT75, KRT79, HBD, HSPA5, JUP, KRT10, KRT17, PPIA, SFN, TPI1, TUBA4A, TXN
Thymus	31	33.0	HSPA1A, MIF, PPIA, TUBA1C, ACTG1, ANXA2, ASAH1, EEF1A1, ENO1, GAPDH, HSPA1A, HSPA5, LDHA, MIF, MYH9, PPIA, PRDX6, S100A11, S100P, SFN, TPI1, YWHAE, ANXA1, CALML3, CAPG, CKB, DSP, GGH, GM2A, HSPB1, JUP
B cells	23	24.5	KRT17, KRT5, LDHA, LGALS3, MIF, MYH9, NME1, PPIA, PRDX6, S100A8, S100A9, SFN, TPI1, TUBA1C, TUBA4A, TUBB, TXN, YWHAE, ACTG1, ANXA2, GAPDH, HSPA5, HSPB1
Keratinocytes	22	23.4	ENO1, GAPDH, HSPA1A, KRT10, TPI1, YWHAE, ACTN4, ANXA1, EEF1A1, HSPA5, KRT1, LDHA, MYH9, TUBA1C, ASAH1, HBD, HRNR, PPIA, PRDX6, MIF, NME1, STX3
Tracheobronchial cells	9	9.6	LGALS3, LRRC15, LYZ, S100A8, S100A9, SELENBP1, STX3, TXN, ACTN4
Intestinal epithelial cells	7	7.4	S100A8, S100A9, SBSN, HBD, ANXA1, ACTG1, ANXA2

Aqueous humor	3	3.2	HSPA5, HSPB1, JUP
Endothelial cells	3	3.2	EEF1A1, ENO1, GAPDH
Plasma	3	3.2	TUBA4A, TUBB, YWHAE
Tabecular meshwork cells	3	3.2	CALM2, CALM3, GAPDH
Amniotic fluid	1	1.1	ANXA1

Table S10: List of 78 prominent metabolites identified in pangolin scale. PS= Proximal region of a scale; DS=Distal region of a scale. Only metabolites presented in all 6 experimental sets were selected for analysis.

HMDB ID	Class	Metabolite	PS1	PS2	PS3	DS1	DS2	DS3
HMDB00070	Amino acids	Pipecolic acid	23442000	40217000	72943000	16285000	10031000	43545000
HMDB00517	Amino acids	L-Arginine	5714900	11187000	20500000	2463400	2130500	10328000
HMDB00191	Amino acids	L-Aspartic acid	6142000	9765400	15420000	2818800	2128900	10152000
HMDB00267	Amino acids	Pyroglutamic acid	3078200	6263500	13035000	2113900	1373900	6295500
HMDB00301	Imidazoles	Urocanic acid	1497700	5472100	10901000	636770	461980	1958400
HMDB00158	Amino acids	L-Tyrosine	1669100	3656100	9182800	985630	802270	3291600
HMDB00159	Amino acids	L-Phenylalanine	1331100	3128500	7145300	1032100	478420	3118200

HMDB00687	Amino acids	L-Leucine	1102200	2648800	6315300	1003700	462940	2661100
HMDB00786	Purine	Oxypurinol	1026700	1410500	2338200	1441000	2101900	1158000
HMDB00162	Amino acids	L-Proline	872860	1708900	3320800	792070	565230	1645800
HMDB00883	Amino acids	L-Valine	609620	1300500	2865100	524420	314310	1368000
HMDB00904	Amino acids	Citrulline	575210	1163400	2733000	173130	89193	1220800
HMDB00156	Beta hydroxy acids	Malic acid	1341700	216520	1811100	911210	271780	406130
HMDB00043	Amino acids	Betaine	1034100	603150	1035600	761200	653980	754180
HMDB00821	Amino acids	Phenylacetylglutamine	618410	505370	1711500	815340	557760	544680
HMDB00929	Amino acids	L-Tryptophan	534020	944740	1298100	470990	493170	511980
HMDB00187	Amino acids	L-Serine	534000	917570	1136700	307270	188710	896950
HMDB00157	Purines	Hypoxanthine	485440	586350	812700	599700	701570	579600
HMDB00062	Quaternary ammonium salts	L-Carnitine	451360	606990	697330	489750	843570	251480
HMDB00251	Amino acids	Taurine	336890	436890	379220	468550	509680	326290
HMDB00182	Amino acids	L-Lysine	186480	466400	1044500	82064	44149	402150
HMDB11172	Peptide	L-gamma-glutamyl-L-valine	154810	364110	1109100	69347	67425	388750

HMDB00254	Dicarboxylic acid	Succinic acid	138570	191960	998770	131000	133480	444720
HMDB00097	Quaternary ammonium salts	Choline	215130	275150	396020	347130	413430	297990
HMDB00190	Alpha hydroxy acids	L-Lactic acid	235720	283900	415840	254890	307520	237900
HMDB00292	Purines	Xanthine	174920	259510	413950	266760	391800	206490
HMDB00167	Amino acids	L-Threonine	174170	418840	493660	122420	85128	411760
HMDB00094	Tricarboxylic acids	Citric acid	83612	136870	1227400	42453	58237	157170
HMDB00625	Carbohydrates	Gluconic acid	169390	185900	593090	104300	156850	215990
HMDB11171	Peptide	L-gamma-glutamyl-L-leucine	100430	196350	685740	35885	34859	226370
HMDB00462	Imidazoles	Allantoin	124320	220270	259630	146740	238490	244100
HMDB00168	Amino acids	L-Asparagine	128720	266130	441280	54479	41129	298200
HMDB01624	Fatty acids	2-Hydroxycaproic acid	73505	98046	407630	88877	167050	349720
HMDB00148	Amino acids	L-Glutamic acid	145570	213460	437160	60669	61798	260530
HMDB00562	Amino acids	Creatinine	133390	191430	171180	199640	274760	81749
HMDB00161	Amino acids	L-Alanine	94693	194750	326810	77357	40229	198010
HMDB00714	Benzoic acids	Hippuric acid	84041	81241	188000	120060	274100	110450

HMDB00086	Glycerophospholipids	Glycerophosphocholine	112480	95327	145910	145120	100450	127080
HMDB01539	Amino acids	Dimethylarginine	35638	128270	387310	20932	12918	135730
HMDB28994	Peptide	Phenylalanyl- Glutamate	51103	110960	404030	11661	11821	127190
HMDB04827	Amino acids	Proline betaine	95314	95012	237980	85124	99779	98221
HMDB29615	Amino Acids	2-Azetidinecarboxylic acid	75321	155130	256730	44329	27109	147900
HMDB00064	Amino acids	Creatine	89020	110690	131370	107160	148960	73170
HMDB00195	Purine nucleosides	Inosine	62759	100780	181800	83405	111190	101930
	Peptide	Tyr Gln Asn	38392	80305	292150	19483	35220	102150
	Peptide	Tyr Cys Val Lys	28387	47320	366190	12582	41892	52290
HMDB11170	Peptide	L-gamma-glutamyl-L- isoleucine	42657	93221	251650	26203	21830	89235
HMDB00296	Pyrimidine nucleosides	Uridine	29226	66033	289760	12516	10980	107260
HMDB01406	Pyridines	Niacinamide	29981	52167	170770	29260	38494	84220
HMDB00289	Purines	Uric acid	33722	55830	126510	26601	40191	71621
HMDB00671	Indolyl carboxylic acids	Indolelactic acid	25698	58311	112300	31735	54483	51976

HMDB00754	Phenols	3-Hydroxyisovaleric acid	25546	33383	100530	29008	43711	61560
HMDB00123	Amino acids	Glycine	30860	66339	84763	22122	17040	56598
HMDB01138	Amino acids	N-Acetylglutamic acid	15215	27255	152590	11261	16953	40094
HMDB00122	Pyrimidines	D-Glucose	29123	50899	89109	18903	23392	51303
	Peptide	Asn Asn Ile Leu	10652	19186	144910	8884	23176	32028
HMDB00008	Alpha hydroxy acids	2-Hydroxybutyric acid	25227	30291	63005	30850	46475	33908
HMDB00134	Carboxylic acids	Fumaric acid	63097	12541	38040	57929	30516	7248
HMDB00045	Purine nucleotides	Adenosine monophosphate	30340	30665	61600	25784	28735	31223
HMDB00512	Amino acids	N-Acetyl-L-phenylalanine	11690	16141	117480	12894	12301	33242
HMDB00619	Bile acids	Cholic acid	58428	9138	68305	24172	9094	26209
HMDB00294	Urea	18420 36592	22204	28833	43408	34544		
HMDB00132	Purines	Guanine	24488	18536	31912	33430	50268	20191
HMDB00299	Purine nucleosides	Xanthosine	14512	19764	31506	18562	22779	27333
	Peptide	Gln Met Ala Pro	9221	19894	63550	4416	5234	27708

HMDB59655	Hydroxy acids	2-Hydroxyglutarate	15584	10237	50483	21725	14063	16435
HMDB00646	Carbohydrates	L-Arabinose	12860	19680	41249	13544	24211	15087
	Peptide	Pro Glin Leu Val	7196	12594	74115	5122	11480	10341
HMDB06293	Carbohydrates	L-Erythrulose	11717	15117	27391	12642	19705	10832
HMDB10383	Glycerophosphocholines	LysoPC(16:0)	17602	13549	18854	17993	12226	17069
HMDB00262	Pyrimidines	Thymine	10692	10560	18123	13864	24497	14134
HMDB00201	Acyl carnitines	L-Acetylcarnitine	7362	11979	44994	5855	3145	11168
HMDB00133	Purine nucleotides	Guanosine	4355	6862	20656	5596	5049	8281
HMDB02243	Pyridines	Picolinic acid	4057	4169	14876	5827	5729	4640
HMDB11745	Amino acids	N-Acetyl-L-methionine	3014	3012	8297	2805	3873	4534
HMDB00300	Pyrimidines	Uracil	2824	2859	7965	3362	2967	3916
HMDB00958	Carboxylic acids	Aconitic acid	2920	2871	5412	2511	2595	2320
HMDB00630	Pyrimidines	Cytosine	2146	2128	3718	2492	4490	2068

Table S11: Screening of 33 metabolites in pangolin scales for antibacterial effects at 12 hours (Mean $\pm$ Standard Error of the Mean (SEM)). Highlighted in bold represent metabolites whose caused bacterial growth rate below 80% used for subsequent MIC assay.

Metabolites	Bacterial growth (%)	
	<i>E. coli</i>	<i>S. aureus</i>
Malic acid	63.81 $\pm$ 6.63	21.48 $\pm$ 1.87
Succinic Acid	83.64 $\pm$ 0.9	28.09 $\pm$ 1.84
Hippuric acid	107.65 $\pm$ 1.23	50.31 $\pm$ 0.18
Fumaric acid	103.97 $\pm$ 3.21	69.17 $\pm$ 3.32
L-Valine	92.34 $\pm$ 0.16	73.56 $\pm$ 5.24
Citric Acid	91.42 $\pm$ 1.09	78.15 $\pm$ 3.31
Glycine	91.64 $\pm$ 0.57	78.65 $\pm$ 0.94
L-Leucine	92.02 $\pm$ 3.67	80 $\pm$ 2.73
L-Threonine	91.33 $\pm$ 1.47	80.31 $\pm$ 3
L-Serine	94.62 $\pm$ 0.26	80.72 $\pm$ 2.33
L-Arabinose	92.11 $\pm$ 2.22	81.11 $\pm$ 2.2
4-Amino-2-hydroxybutyricacid	94.38 $\pm$ 2.56	82.5 $\pm$ 3.9
N-Acetyl-L-Methionine	91.77 $\pm$ 2.32	82.58 $\pm$ 2.76
Urea	100.4 $\pm$ 2.71	82.58 $\pm$ 2.76
L-Proline	92.78 $\pm$ 1.28	82.89 $\pm$ 3.89
L-Alanine	92.07 $\pm$ 2.69	82.95 $\pm$ 3.91
N-Acetyl-L-Phenylalanin	90.36 $\pm$ 1.88	83.86 $\pm$ 2.31
Taurine	91.46 $\pm$ 3.35	83.86 $\pm$ 2.37
L-Glutamic acid	104.34 $\pm$ 2.19	84.64 $\pm$ 4.11
L-Citrulline	95.01 $\pm$ 1.64	84.99 $\pm$ 3.95
Betaine	95.73 $\pm$ 2.17	85.58 $\pm$ 2.29
Gluconic acid	92.4 $\pm$ 1.96	86.6 $\pm$ 4.49
Thymine	93.34 $\pm$ 2.64	89.16 $\pm$ 0.87

Creatinine	89.76 ± 1.01	89.43 ± 3.34
Cytosine	99.79 ± 7.28	90.38 ± 6.86
L-Asparagine	96.19 ± 2.42	90.7 ± 7.18
L-Lysine	94.78 ± 3.02	92.57 ± 4.54
Allantoin	92.01 ± 5.6	98.66 ± 6.01
L-Tryptophan	104.77 ± 3.19	100.35 ± 2.29
Uracil	101.58 ± 2.61	102.24 ± 2.06
L-Carnitine	95.34 ± 2.21	102.68 ± 4.63
L-Pipecolic acid	91.07 ± 2.59	107.9 ± 3.19

Table S12: Minimum inhibitory concentration (MIC) of metabolite or combination of metabolite against *E. coli* and *S. aureus*.

Metabolite or Combination of Metabolite	MIC	
	<i>E. coli</i>	<i>S. aureus</i>
Fumaric Acid	2.5 C	2.5 C
Succinic Acid	C	C
Malic Acid	0.25 C	0.25 C
Citric Acid	1.25 C	1.25 C
L-Valine	2.5 C	2.5 C
Glycine	10 C	10 C
Hippuric Acid	C	C
Malic Acid +Fumaric Acid	0.2 C	0.2 C
Malic Acid +Succinic Acid	0.2 C	0.2 C
Malic Acid +Citric Acid	0.2 C	0.2 C
Malic Acid +L-Valine	0.2 C	0.2 C
Malic Acid +Glycine	0.2 C	0.2 C
Malic Acid +Hippuric Acid	0.2 C	0.2 C
Malic Acid +Fumaric Acid +Succinic Acid	0.2 C	0.2 C
Malic Acid +Fumaric Acid +L-Valine	0.4 C	0.4 C
Malic Acid +Fumaric Acid +Citric Acid	0.4 C	0.4 C
Malic Acid +Fumaric Acid +Glycine	0.2 C	0.2 C
Malic Acid +Fumaric Acid +Hippuric Acid	0.2 C	0.2 C
Malic Acid +Succinic Acid +L-Valine	0.2 C	0.2 C
Malic Acid +Succinic Acid +Citric Acid	0.2 C	0.2 C
Malic Acid +Succinic Acid +Glycine	0.2 C	0.2 C
Malic Acid +Succinic Acid +Hippuric Acid	0.2 C	0.2 C
Malic Acid +L-Valine +Citric Acid	0.2 C	0.2 C
Malic Acid +L-Valine +Glycine	0.4 C	0.4 C
Malic Acid +L-Valine +Hippuric Acid	0.4 C	0.4 C

Malic Acid +Glycine +Hippuric Acid	0.2 C	0.2 C
Malic Acid +Glycine +Citric Acid	0.2 C	0.4 C
Malic Acid +Hippuric Acid +Citric Acid	0.1 C	0.2 C
Malic Acid +Fumaric Acid +Succinic Acid +L-Valine	0.2 C	0.2 C
Malic Acid +Fumaric Acid +Succinic Acid +Citric Acid	0.2 C	0.2 C
Malic Acid +Fumaric Acid +Succinic Acid +Glycine	0.2 C	0.2 C
Malic Acid +Fumaric Acid +Succinic Acid +Hippuric Acid	0.2 C	0.2 C
Malic Acid +Fumaric Acid +L-Valine +Citric Acid	0.2 C	0.2 C
Malic Acid +Fumaric Acid +L-Valine +Glycine	0.4 C	0.4 C
Malic Acid +Fumaric Acid +L-Valine +Hippuric Acid	0.2 C	0.2 C
Malic Acid +Fumaric Acid +Citric Acid +Glycine	0.2 C	0.2 C
Malic Acid +Fumaric Acid +Citric Acid +Hippuric Acid	0.2 C	0.2 C
Malic Acid +Fumaric Acid +Glycine +Hippuric Acid	0.1 C	0.1 C
Malic Acid +Succinic Acid +L-Valine +Citric Acid	0.2 C	0.2 C
Malic Acid +Succinic Acid +L-Valine +Glycine	0.2 C	0.2 C
Malic Acid +Succinic Acid +L-Valine +Hippuric Acid	0.2 C	0.2 C
Malic Acid +Succinic Acid +Citric Acid +Glycine	0.2 C	0.2 C
Malic Acid +Succinic Acid +Citric Acid +Hippuric Acid	0.2 C	0.2 C
Malic Acid +Succinic Acid +Glycine +Hippuric Acid	0.2 C	0.2 C
Malic Acid +L-Valine +Citric Acid +Glycine	0.4 C	0.4 C
Malic Acid +L-Valine +Citric Acid +Hippuric Acid	0.2 C	0.2 C
Malic Acid +L-Valine +Glycine +Hippuric Acid	0.4 C	0.4 C
Malic Acid +Citric Acid +Glycine +Hippuric Acid	0.1 C	0.1 C
Malic Acid +Fumaric Acid +Succinic Acid +L-Valine +Citric Acid	0.2 C	0.2 C
Malic Acid +Fumaric Acid +Succinic Acid +L-Valine +Glycine	0.2 C	0.2 C

Malic Acid +Fumaric Acid +Succinic Acid +L-Valine +Hippuric Acid	0.1 C	0.2 C
Malic Acid +Fumaric Acid +L-Valine +Citric Acid +Glycine	0.2 C	0.2 C
Malic Acid +Fumaric Acid +L-Valine +Citric Acid +Hippuric Acid	0.1 C	0.1 C
Malic Acid +Fumaric Acid +L-Valine +Glycine +Hippuric Acid	0.1 C	0.2 C
Malic Acid +Fumaric Acid +Citric Acid +Glycine +Hippuric Acid	0.1 C	0.1 C
Malic Acid +Succinic Acid +L-Valine +Citric Acid +Glycine	0.2 C	0.2 C
Malic Acid +Succinic Acid +L-Valine +Citric Acid +Hippuric Acid	0.1 C	0.1 C
Malic Acid +Succinic Acid +L-Valine +Glycine +Hippuric Acid	0.1 C	0.1 C
Malic Acid +Succinic Acid +Citric Acid +Glycine +Hippuric Acid	0.1 C	0.1 C
Malic Acid +L-Valine +Citric Acid +Glycine +Hippuric Acid	0.1 C	0.2 C
Malic Acid +Succinic Acid +L-Valine +Citric Acid +Glycine +Hippuric Acid	0.1 C	0.1 C
Malic Acid +Fumaric Acid +L-Valine +Citric Acid +Glycine +Hippuric Acid	0.1 C	0.1 C
Malic Acid +Fumaric Acid +Succinic Acid +Citric Acid +Glycine +Hippuric Acid	0.1 C	0.1 C
Malic Acid +Fumaric Acid +Succinic Acid +L-Valine +Glycine +Hippuric Acid	0.1 C	0.1 C

Malic Acid +Fumaric Acid +Succinic Acid +L-Valine		
+Citric Acid +Hippuric Acid	0.1 C	0.1 C
Malic Acid +Fumaric Acid +Succinic Acid +L-Valine		
+Citric Acid +Glycine	0.1 C	0.1 C
Malic Acid +Fumaric Acid +Succinic Acid +L-Valine		
+Citric Acid +Glycine +Hippuric Acid	0.1 C	0.1 C

Table S13: Minimum Bactericidal Concentration (MBC) of metabolite combination against *E. coli* and *S. aureus*.

Metabolite Combination	MBC	
	<i>E. coli</i>	<i>S. aureus</i>
Malic Acid +Fumaric Acid +Glycine +Hippuric Acid	0.4C	0.4C

Table S14: List of 70 metabolites identified on the skin surface of pangolins. Criteria: metabolites presented in all three experimental sets.

HMDB ID	Class	Metabolite	S1	S2	S3
HMDB29615	Amino Acids	2-Azetidinecarboxylic acid	5907	4440	11189
HMDB00958	Carboxylic acids	Aconitic acid	1789	1715	1821
HMDB00517	Amino acids	L-Arginine	24529	16553	20422
HMDB00168	Amino acids	L-Asparagine	3227	2757	3277
HMDB00043	Amino acids	Betaine	1.15E+05	82054	90603
HMDB00062	Quaternary ammonium salts	L-Carnitine	25380	7707	9559
HMDB00097	Quaternary ammonium salts	Choline	11991	4924	3654
HMDB00904	Amino acids	Citrulline	1222	733	894
HMDB00064	Amino acids	Creatine	1.10E+05	93350	2.47E+05
HMDB00562	Amino acids	Creatinine	9317	7385	17768
HMDB00630	Pyrimidines	Cytosine	270	190	276
HMDB00122	Pyrimidines	D-Glucose	8400	3398	4651

HMDB00148	Amino acids	L-Glutamic acid	3090	1236	1832
HMDB00086	Glycerophospholipids	Glycerophosphocholine	93150	34498	24363
HMDB00132	Purines	Guanine	4425	3186	3009
HMDB00133	Purine nucleotides	Guanosine	650	287	322
HMDB00157	Purines	Hypoxanthine	51018	32119	32005
HMDB00201	Acyl carnitines	L-Acetylcarnitine	4875	2055	2153
HMDB00161	Amino acids	L-Alanine	483	246	234
HMDB11170	Peptide	L-gamma-glutamyl-L- isoleucine	1779	1791	2626
HMDB11171	Peptide	L-gamma-glutamyl-L- leucine	4030	4969	6989
HMDB00687	Amino acids	L-Leucine	4102	2905	3340
HMDB00162	Amino acids	L-Proline	9186	6706	8152
HMDB00182	Amino acids	L-Lysine	634	556	532
HMDB10383	Glycerophosphocholines	LysoPC(16:0)	25784	14286	9367
HMDB01406	Pyridines	Niacinamide	2009	1184	1340
HMDB00159	Amino acids	L-Phenylalanine	3575	2382	2926

HMDB04827	Amino acids	Proline betaine	2616	1833	2339
HMDB00267	Amino acids	Pyroglutamic acid	92471	70886	88820
HMDB00187	Amino acids	L-Serine	724	255	456
HMDB00167	Amino acids	L-Threonine	625	303	494
HMDB00262	Pyrimidines	Thymine	165	171	200
HMDB00929	Amino acids	L-Tryptophan	2.45E+05	2.18E+05	2.54E+05
HMDB00158	Amino acids	L-Tyrosine	3429	2096	2439
HMDB00300	Pyrimidines	Uracil	663	450	296
HMDB00296	Pyrimidine nucleosides	Uridine	1956	1640	1543
HMDB00883	Amino acids	L-Valine	32549	30959	31567
HMDB00292	Purines	Xanthine	8255	5682	6308
HMDB00008	Alpha hydroxy acids	2-Hydroxybutyric acid	5510	5288	5603
HMDB01624	Fatty acids	2-Hydroxycaproic acid	28284	28094	25272
HMDB59655	Hydroxy acids	2-Hydroxyglutarate	2508	2380	2934
HMDB00754	Phenols	3-Hydroxyisovaleric acid	12696	12012	12705

HMDB00045	Purine nucleotides	Adenosine monophosphate	18003	15279	22219
HMDB00462	Imidazoles	Allantoin	1509	3158	2887
HMDB00094	Tricarboxylic acids	Citric acid	19073	13998	23802
HMDB00191	Amino acids	L-Aspartic acid	2.55E+05	85389	2.00E+05
HMDB00134	Carboxylic acids	Fumaric acid	1455	1558	1546
HMDB00625	Carbohydrates	Gluconic acid	7444	5025	7079
HMDB00714	Benzoic acids	Hippuric acid	823	1166	1265
HMDB00671	Indolyl carboxylic acids	Indolelactic acid	533	588	747
HMDB00195	Purine nucleosides	Inosine	21458	42656	61152
HMDB00190	Alpha hydroxy acids	L-Lactic acid	69495	84020	93121
HMDB00646	Carbohydrates	L-Arabinose	583	767	838
HMDB06293	Carbohydrates	L-Erythrulose	802	882	1263
HMDB00156	Beta hydroxy acids	Malic acid	5183	5710	6988
HMDB01138	Amino acids	N-Acetylglutamic acid	1020	909	1453
HMDB00512	Amino acids	N-Acetyl-L- phenylalanine	1510	2207	2290

HMDB00786	Purine	Oxypurinol	12067	12598	18523
HMDB00821	Amino acids	Phenylacetylglycine	52476	9777	54800
HMDB00070	Amino acids	Pipecolic acid	1.37E+05	22791	1.12E+05
HMDB00254	Dicarboxylic acid	Succinic acid	6167	6411	9260
HMDB00251	Amino acids	Taurine	12459	34913	33878
HMDB00289	Purines	Uric acid	4547	4484	7765
HMDB00288	Pyrimidine nucleotides	Uridine 5'-monophosphate	3868	4019	6491
HMDB00299	Purine nucleosides	Xanthosine	2495	2891	4744
	Peptide	Tyr Cys Val Lys	7848	3191	4371
	Peptide	Glin Met Ala Pro	1281	721	851
	Peptide	Tyr Glin Asn	6503	2743	3717
	Peptide	Asn Asn Iie Leu	5044	10276	15166
	Peptide	Pro Glin Leu Val	3197	3418	2509

Table S15: List of 12 differentially expressed metabolites between scale and skin.

Metabolite	Fold Enrichment (Scale/Skin)	P-value
Taurine	14.2	0.004
Creatinine	14.4	0.010
L-Carnitine	41.2	0.015
Hypoxanthine	16.4	0.025
Guanine	7.1	0.030
Betaine	9.3	0.031
Choline	43.1	0.032
Thymine	73.5	0.035
Allantoin	80.0	0.038
L-Serine	1803.7	0.039
Cytosine	10.9	0.044
L-Lactic acid	3.8	0.049

Table S16: List of 14 proteins identified on the skin surface of pangolins.

ID	Protein identification probability	Exclusiv e unique peptide count	Exclusiv e unique spectrum count	Total spectrum count	Gene Description	Gene Symbol	Molecular Weight	Accession Number
MMP0022578	100.00%	20	24	36	keratin 1	KRT1	63 kDa	AFA52003.1
MMP0022283	100.00%	14	20	29	keratin, type I cytoskeletal 10	KRT10	49 kDa	NP_000412.3
MMP0017552	100.00%	10	10	17	keratin, type II cuticular Hb5 isoform 1	KRT85	61 kDa	NP_002274.1
MMP0019724	100.00%	7	7	8	serum albumin	HAS	68 kDa	AAN17825.1
MMP0020663	100.00%	5	6	6	protein S100-A9	S100A9	14 kDa	NP_002956.1
MMP0020662	100.00%	4	5	6	protein S100-A12	S100A12	11 kDa	NP_005612.1
MMP0001835	100.00%	4	4	4	hCG1795014	hCG179501	23 kDa	EAW50553.1

MMP0013009	99.93%	1	1	7	keratin, type I KRT17	141 kDa	NP_000413.1
					cytoskeletal 17		
MMP0010956	97.50%	1	1	2	actin, cytoplasmic 2 ACTG1	44 kDa	NP_001186883.1
MMP0006735	99.45%	2	2	2	delta-globin HBD	17 kDa	AAL72117.1
MMP0022581	70.3%	2	2	5	keratin, type II KRT5	52 kDa	NP_000415.2
					cytoskeletal 5		
MMP0022587	99.9%	2	2	4.5	keratin 4 KRT4	155 kDa	EAW96647.1
MMP0001194	94.35%	1	1	1	calmodulin-3 CALM3	17 kDa	NP_001316851.1
					isoform 1		
MMP0001084	100.00%	3	3	3	lysozyme C LYZ	12 kDa	NP_000230.1

Notes:

Protein Identification Probability=Scaffold's calculated probability that the protein identification for any of the MS Samples is correct. Results are color-coded to indicate significant differences in protein identification confidence.

Exclusive Unique Peptide Count= The number of different amino acid sequences, regardless of any modification that are associated with a single protein group.

Exclusive Unique Spectrum Count=Number of distinct spectra associated only with a single protein group.

Total Spectrum Count=The total number of spectra associated to a single protein group, including those shared with other proteins.