Table S1. Summary of clinical scores (VAS and SCORAD) and laboratory findings in DOCK8 deficient and atopic dermatitis cohorts.

Abbreviations: AD atopic dermatitis, DOCK8 dedicator of cytokinesis, F female, M male, SCORAD (severity scoring of atopic dermatitis), SEM standard error of the mean, VAS (visual analogue score).

Diagnosis	Patient code	Mutation	Age (Y)	Sex (M/F)	IgE Levels (KU/L)	RBC 10^ 12/L	WBC 10^9/L	Eosinophils 10^9/L	CD4/CD8 Ratio	VAS	SCORAD
DOCK8	**P1**	**NM_203447.3:c.[2606-1G>A; c.405_827del]**	**21**	**F**	25000	0.01	9.2	24.8	2.1	15	68.7
	P2	NM_203447.3:c.[2606-1G>A; c.405_827del]	16	M	9140	4.17	3.72	35	0.8	13	67
	P3	NM_203447.3:c.5625T>G:p.Y1875	16	F	1690	4.2	4.63	50.3	1	14	59.8
	P4	NM_203447:c.827+6T>C	16	F	11240	5.9	4.9	11.4	0.73	15	77.4
	P5	NM_203447.3:c.5962_6068del	7	M	10170	5.29	9.93	26.4	0.7	17	79.5
	P6	NM_001193536:c.3949+1G>T	14	M	15550	6.82	4.46	11.7	1.3	15	62.5
	P7	NM_001193536:c.1593+1G>T	4	M	86940	5.3	24.9	31.4	9	17	70.6
	P8	NM_001193536:c.1593+1G>T	9	F	44630	5.26	12.49	34.8	8.1	9	58.2
	P9	NM_001190458:c.1905_1905+1delGG	8	F	26340	3.81	21.42	35.1	3.2	14	58.8
	P10	NM_203447.3:c.5625T>G:p.Y1875	21	M	265	4.7	9.7	12	1.1	12	70.1
Average±SEM			**13.2±5.9**	**5/5 (M/F)**	**19817.30±4772.6**	**4.5±0.57**	**10.53±2.3**	**27.29±4.02**	**2.8±0.99**	**14.1±0.75**	**67.26 ±2.37**
ATOPIC DERMATITIS	P11	**DOCK8 mutation negative**	6	M	6540	5.2	10.6	16.5	0.9	16	64.4
	P12		15	M	16500	6.39	3.72	15.6	1.4	14	71.3
	P13		10	M	1612	5.48	8.01	13.9	1.2	16	73.3
	P14		3	M	839	5.3	6.59	6.7	_	13	56.1
	P15		8	M	1221	4.9	5.09	13	1.5	9	40.8
	P16		13	M	659	5.2	5.15	13	1.2	10	54.9
	P17		15	F	1387	4.71	9.63	12.3	1.4	15	75
	P18		16	M	365	5.15	2.71	7.9	2.3	14	65.1
	P19		12	M	4587	5.66	9.2	5.1	1.5	16	70.6
Average±SEM			**10.8±1.4**	**8/1 (M/F)**	**5288.20±1736.3**	**5.33±0.16**	**6.74±0.92**	**27.29±1.3**	**1.43±0.14**	**13.6±0.86**	**63.5 ± 3.702**

Table S2: Positively identified metabolites that have been significantly changed between the DOCK8 deficient patients and healthy controls. q-value< 0.05

HMDB ID	Name	Mass (m/z)	Retention time (min)	Fold change	p-value
316	Phenyl-Leucine	278.1631	15.9	0.395278	0.000060
HMDB00020	p-Hydroxyphenylacetic acid	152.0473	16.91	1.665532	0.000897
HMDB00070	D-Pipecolic acid	129.079	13.23	1.587058	0.000212
HMDB00112	Gamma-Aminobutyric acid	103.0633	7.79	1.534256	0.000000
HMDB00133	Guanosine	283.0917	2.22	4.122263	0.000001
HMDB00206	N6-Acetyl-L-Lysine	188.1161	5.71	1.681203	0.000000
HMDB00210	Pantothenic acid	219.1107	8.37	1.832101	0.000000
HMDB00224	O-Phosphoethanolamine	141.0191	2.02	0.582280	0.000076
HMDB00251	Taurine	125.0147	2.24	0.628275	0.000000
HMDB00259	Serotonin	176.095	24.65	1.815646	0.000003
HMDB00271	Sarcosine	89.0477	9.34	1.573576	0.000000
HMDB00300	Uracil	112.0273	11.34	2.245593	0.000003
HMDB00440	3-Hydroxyphenylacetic acid	152.0473	16.72	1.665532	0.000897
HMDB00450	5-Hydroxylysine	162.1004	13.88	2.087091	0.000000
HMDB00452	L-Alpha-aminobutyric acid	103.0633	9.13	2.122152	0.000000
HMDB00469	5-Hydroxymethyluracil	142.0378	8.87	0.661088	0.000001
HMDB00500	4-Hydroxybenzoic acid	138.0317	17.57	0.481133	0.032552
HMDB00500	4-Hydroxybenzoic acid	138.0317	17.57	0.497054	0.000000
HMDB00669	Ortho-Hydroxyphenylacetic acid	152.0473	16.42	1.665532	0.000897
HMDB00684	L-Kynurenine	208.0848	11.44	1.744385	0.000000
HMDB00706	L-Aspartyl-L-phenylalanine	280.1059	10.07	0.315026	0.000011
HMDB00716	L-Pipecolic acid	129.079	13.45	1.587058	0.000212
HMDB00750	3-Hydroxymandelic acid	168.0423	21.64	1.586043	0.000000
HMDB00965	Hypotaurine	109.0197	2.47	0.437627	0.000024
HMDB01123	2-Aminobenzoic acid	137.0477	16.62	3.014851	0.000000
HMDB01232	4-Nitrophenol	139.0269	23.45	1.730548	0.000000
HMDB01414	1,4-diaminobutane	88.1	21.27	2.039329	0.000000
HMDB01476	3-Hydroxyanthranilic acid	153.0426	18.14	1.808715	0.000000
HMDB01906	2-Aminoisobutyric acid	103.0633	8.91	2.122152	0.000000
HMDB01918	Thyroxine	776.6867	27.74	1.639578	0.000000
HMDB02064	N-Acetylputrescine	130.1106	7.25	2.196515	0.000000
HMDB02390	3-Cresotinic acid	152.0473	16.8	1.665532	0.000897
HMDB03012	Aniline	93.0578	17.32	2.035166	0.000000
HMDB03334	Symmetric dimethylarginine	202.143	3.05	1.924655	0.000000
HMDB03355	5-Aminopentanoic acid	117.079	8.68	1.622041	0.000751

HMDB03911	3-Aminoisobutanoic acid	103.0633	8.67	2.122152	0.000000
HMDB03911	3-Aminoisobutanoic acid	103.0633	16.29	1.943611	0.000000
HMDB13302	Phenylalanylphenylalanine	312.1474	16.55	0.529397	0.000000
HMDB28848	Glycyl-Phenylalanine	222.1004	11.65	0.597854	0.000037
HMDB28854	Glycyl-Valine	174.1004	9.19	0.266569	0.001304

Table S3. Positively identified metabolites that have been significantly changed between AD and Control, q-value<0.05.

HMDB ID	Name	Mass (m/z)	Retention time (min)	Fold change	p-value
316	Phenyl-Leucine	278.1631	15.9	0.221546	0.000008
HMDB00130	Homogentisic acid	168.0423	24.84	0.512373	0.000003
HMDB00133	Guanosine	283.0917	2.22	6.402693	0.000000
HMDB00148	L-Glutamic Acid	147.0532	5.05	0.534262	0.000000
HMDB00152	Gentisic acid	154.0266	17.11	0.546813	0.015066
HMDB00191	L-Aspartic Acid	133.0375	5.16	0.639508	0.000498
HMDB00210	Pantothenic acid	219.1107	8.37	1.539231	0.000000
HMDB00214	Ornithine	132.0899	16.58	0.579056	0.000000
HMDB00224	O-Phosphoethanolamine	141.0191	2.02	0.570539	0.000095
HMDB00251	Taurine	125.0147	2.24	0.620118	0.000000
HMDB00259	Serotonin	176.095	24.65	2.828641	0.000000
HMDB00440	3-Hydroxyphenylacetic acid	152.0473	16.72	0.660876	0.021910
HMDB00450	5-Hydroxylysine	162.1004	13.88	2.452587	0.000000
HMDB00452	L-Alpha-aminobutyric acid	103.0633	9.13	1.775709	0.000001
HMDB00500	4-Hydroxybenzoic acid	138.0317	17.57	0.533774	0.035612
HMDB00517	L-Arginine	174.1117	2.44	1.616970	0.000000
HMDB00669	Ortho-Hydroxyphenylacetic acid	152.0473	16.42	0.660876	0.021910
HMDB00706	L-Aspartyl-L-phenylalanine	280.1059	10.07	0.189421	0.000002
HMDB00725	Trans-4-Hydroxyl-L-Proline	131.0582	5.17	1.556155	0.000026
HMDB00750	3-Hydroxymandelic acid	168.0423	21.64	1.571945	0.000000
HMDB00991	2-aminooctanoic acid	159.1259	19.2	2.092571	0.000000
HMDB01123	2-Aminobenzoic acid	137.0477	16.62	1.989600	0.000000
HMDB01232	4-Nitrophenol	139.0269	23.45	1.665664	0.000000
HMDB01336	3,4-Dihydroxybenzeneacetic acid	168.0423	23.9	1.667841	0.000002
HMDB01414	1,4-diaminobutane	88.1	21.27	1.802736	0.000000
HMDB01856	Protocatechuic acid	154.02661	24.51	0.560951	0.052173
HMDB01906	2-Aminoisobutyric acid	103.0633	8.91	1.775709	0.000001
HMDB01918	Thyroxine	776.6867	27.74	1.624100	0.000000
HMDB02064	N-Acetylputrescine	130.1106	7.25	1.798382	0.000000
HMDB02390	3-Cresotinic acid	152.0473	16.8	0.660876	0.021910
HMDB03012	Aniline	93.0578	17.32	3.125674	0.000953
HMDB03334	Symmetric dimethylarginine	202.143	3.05	1.823252	0.000000
HMDB03355	5-Aminopentanoic acid	117.079	8.68	1.623791	0.000000
HMDB03911	3-Aminoisobutanoic acid	103.0633	8.67	1.775709	0.000001
HMDB13243	Leucyl-phenylalanine	278.163	16.59	1.759358	0.000002
HMDB13302	Phenylalanylphenylalanine	312.1474	16.55	0.362381	0.000000
HMDB28854	Glycyl-Valine	174.1004	9.19	0.096747	0.000328

Table S4. identified metabolites that have been significantly changed between the DOCK8 deficient and AD patients. q-value< 0.05.

HMDB ID	Name	Mass (m/z)	Retention time (min)	Fold change	p-value
HMDB00133	Guanosine	283.0917	2.22	1.553199	0.006757

HMDB00191	L-Aspartic Acid	133.0375	5.16	0.552161	0.005203
HMDB00965	Hypotaurine	109.0197	2.47	1.898281	0.000833
HMDB00991	2-aminooctanoic acid	159.1259	19.2	1.550839	0.005658
HMDB01476	3-Hydroxyanthranilic acid	153.0426	18.14	0.624233	0.000955
HMDB13243	Leucyl-phenylalanine	278.163	16.59	2.415599	0.000005
HMDB28848	Glycyl-Phenylalanine	222.1004	11.65	2.091982	0.000525

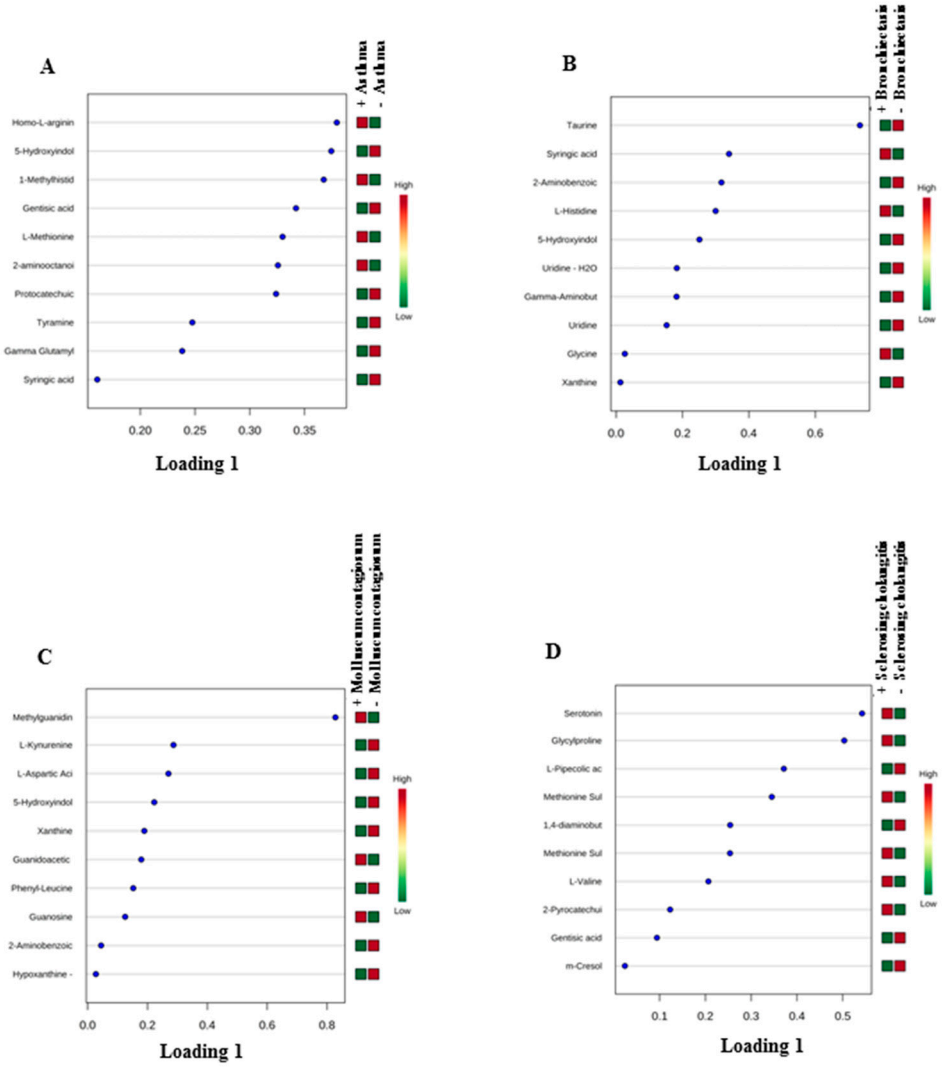

Figure S1A. PLS-DA loading plots based on binary comparisons in DOCK8-deficient patients with (+) and without (-) various clinical phenotypes including (**A**) Asthma, (**B**) Bronchiectasis, (**C**) Molluscum contagiosum, (**D**) Sclerosing cholangitis.

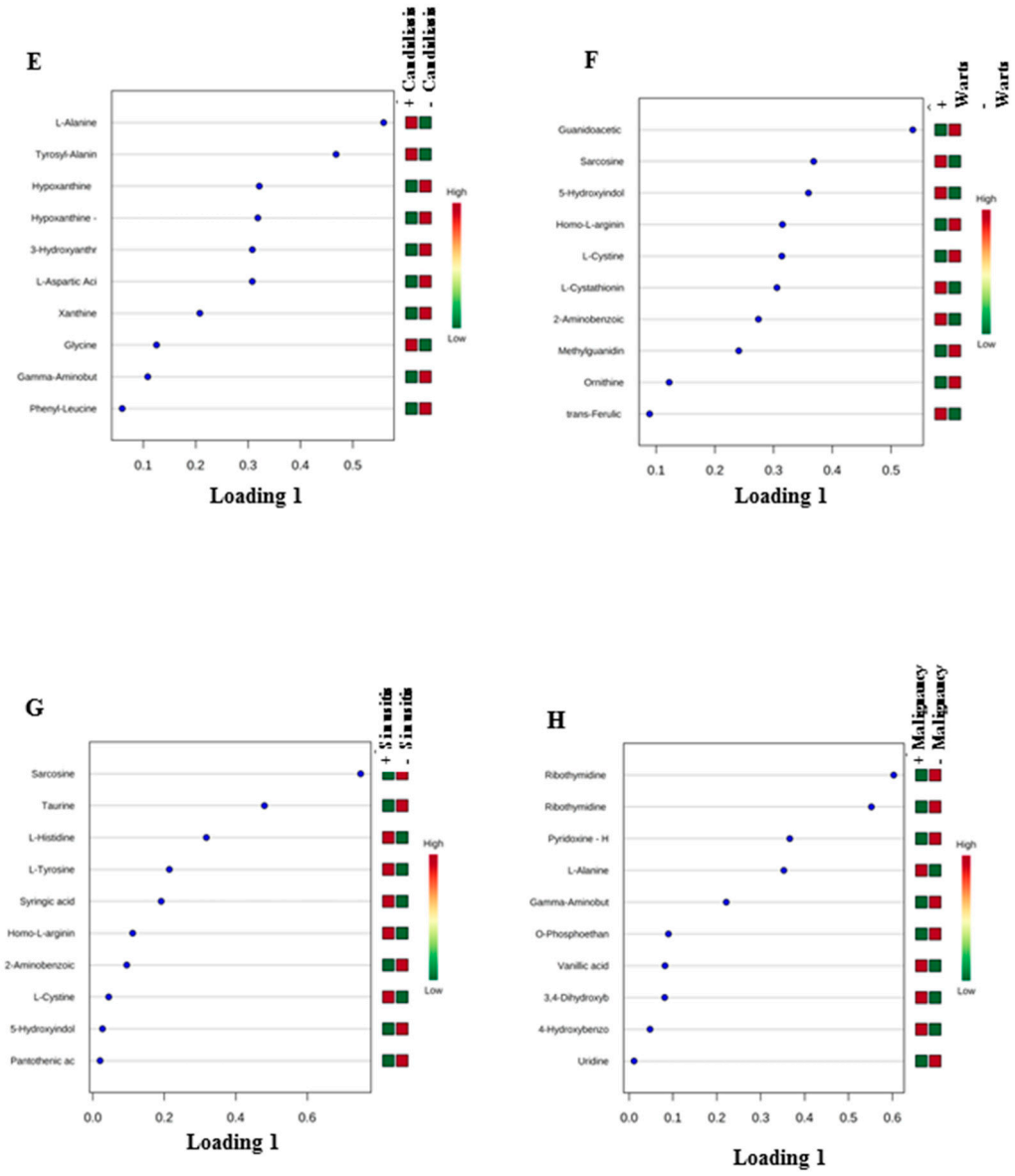

Figure S1B. PLS-DA loading plots based on binary comparisons in DOCK8-deficient patients with (**+**) and without (**-**) various clinical phenotypes including (**E**) Candidiasis, (**F**) Warts, (**G**) Sinusitis, (**H**) Malignancy.