

Supplemental data chapter 7

Serum biomarker profiles demonstrate that atopic dermatitis is a systemic disease

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Table S1. Summary of serum mediators that are differentially upregulated in atopic dermatitis versus healthy controls.

Variables where AD>HC	Healthy controls (n=30)	Moderate AD (n=95)	Severe AD (n=98)
Serum Ig targeting alpha toxin^{GM}	11.2 ^{<Mod,Sev} (7, 18)	75.7 ^{<HC} (62, 92)	99.4 ^{<HC} (77.5, 127.5)
Apelin^{Med}	4.7x10 ^{4<Mod,Sev} (3.8x10 ⁴ , 5.2x10 ⁴)	6.3x10 ^{4>HC} (5.8x10 ⁴ , 6.7x10 ⁴)	6.4x10 ^{4>HC} (5.8x10 ⁴ , 6.6x10 ⁴)
C5a^{GM}	5.2x10 ^{4<Mod,Sev} (4.3x10 ⁴ , 6.3x10 ⁴)	1.3x10 ^{5>HC} (1.1x10 ⁵ , 1.5x10 ⁵)	1.1x10 ^{5>HC} (9.4x10 ⁴ , 1.3x10 ⁵)
Cathepsin B^M	9.9x10 ^{3<Mod,Sev} (8.5x10 ³ , 1.1x10 ⁴)	1.6x10 ^{4>HC} (1.5x10 ⁴ , 1.8x10 ⁴)	1.7x10 ^{4>HC} (1.5x10 ⁴ , 1.8x10 ⁴)
Cystatin C^{Med}	1.2x10 ^{5<Mod,Sev} (8.4x10 ⁴ , 1.5x10 ⁵)	1.9x10 ^{5>HC} (1.7x10 ⁵ , 2.2x10 ⁵)	2.0x10 ^{5>HC} (1.7x10 ⁵ , 2.2x10 ⁵)
Elastase^{Med}	1.2x10 ^{4<Mod,Sev} (7.1x10 ³ , 1.6x10 ⁴)	2.3x10 ^{4>HC} (1.1x10 ⁴ , 8.6x10 ⁴)	3.2x10 ^{4>HC} (1.5x10 ⁴ , 8.6x10 ⁴)
ENA-78^{Med}	7.4x10 ^{2<Mod,Sev} (4.8x10 ² , 1.2x10 ³)	2.4x10 ^{3>HC} (1.6x10 ³ , 3.8x10 ³)	2.7x10 ^{3>HC} (1.9x10 ³ , 4.2x10 ³)
Endoglin^{GM}	1.2x10 ^{3<Mod,Sev} (1.1x10 ³ , 1.3x10 ³)	2.7x10 ^{3>HC} (2.5x10 ³ , 3.0x10 ³)	2.6x10 ^{3>HC} (2.4x10 ³ , 2.9x10 ³)
Eotaxin-1^{GM}	73.6 ^{<Mod,Sev} (61, 88)	525.3 ^{>HC} (439, 629)	610.5 ^{>HC} (509, 733)
Fas^{GM}	840.9 ^{<Mod,Sev} (721, 978)	1889.4 ^{>HC} (1756, 2033)	1987.3 ^{>HC} (1846, 2140)
GCP-2^{GM}	64.2 ^{<Mod,Sev} (34, 120)	148.7 ^{>HC} (121, 182)	147.6 ^{>HC} (119, 183)
GCSF^{Med}	1.8x10 ^{1<Mod,Sev} (1.8x10 ¹ , 1.8x10 ¹)	8.7x10 ^{3>HC} (6.2x10 ³ , 1.7x10 ⁴)	8.6x10 ^{3>HC} (6.2x10 ³ , 1.5x10 ⁴)
HGF^{GM}	629.1 ^{<Mod,Sev} (522, 759)	935.5 ^{>HC} (868, 1009)	1036.4 ^{>HC} (950, 1130)
ICAM-1^{Med}	2.9x10 ^{5<Mod,Sev} (2.2x10 ⁵ , 3.4x10 ⁵)	4.7x10 ^{5>HC} (3.7x10 ⁵ , 6.0x10 ⁵)	5.0x10 ^{5>HC} (4.0x10 ⁵ , 6.7x10 ⁵)
IFN-α^{Med}	0.7 ^{<Mod,Sev} (1, 3)	82.5 ^{>HC} (53, 99)	81.9 ^{>HC} (48, 98)
IL-1α^{Med}	4.7 ^{<Mod,Sev} (3, 8)	23.8 ^{>HC} (9, 39)	26.0 ^{>HC} (14, 53)
IL-1β^{GM}	1.1 ^{<Mod,Sev} (1, 2)	12.5 ^{>HC} (11, 15)	14.4 ^{>HC} (12, 17)
IL-1R1^{Med}	5.6 ^{<Mod,Sev} (3, 8)	76.2 ^{>HC} (39, 114)	79.1 ^{>HC} (52, 118)
IL-1R2^{Med}	1473.4 ^{<Sev} (842, 2060)	1615.2 (1218, 2126)	2002.6 ^{>HC} (1509, 2624)
IL-3^{Med}	2.5 ^{<Mod,Sev} (3, 3)	2.5 ^{>HC} (3, 420)	2.5 ^{>HC} (3, 339)
IL-4^{Med}	0.3 ^{<Mod,Sev} (0, 0)	3.6 ^{>HC} (2, 7)	3.7 ^{>HC} (2, 8)
IL-5^{Med}	5.0 ^{<Mod,Sev} (3, 10)	196.6 ^{>HC} (164, 236)	220.1 ^{>HC} (191, 254)
IL-6^{Med}	1.4 ^{<Mod,Sev} (1, 10)	18.3 ^{>HC} (10, 47)	18.4 ^{>HC} (8, 36)
IL-7^M	5.2 ^{<Mod,Sev} (4, 7)	35.4 ^{>HC} (32, 38)	38 ^{>HC} (34, 41)
IL-9^{GM}	12.2 ^{<Mod,Sev} (5, 31)	76.4 ^{>HC} (60, 98)	93 ^{>HC} (75, 116)
IL-10^{Med}	1.7 ^{<Mod} (2, 2)	1.7 ^{>HC} (2, 8)	1.7 (2, 7)
IL-11^{Med}	4.0 ^{<Mod,Sev} (4, 4)	19.7 ^{>HC} (4, 89)	30.6 ^{>HC} (4, 89)
IL-12^{Med}	3.3 ^{<Mod,Sev} (3, 12)	58.3 ^{>HC} (29, 109)	58.5 ^{>HC} (38, 104)

IL-13^{GM}	23.3 ^{<Mod,Sev} (10, 53)	62.6 ^{>HC} (54, 73)	67.7 ^{>HC} (58, 79)
IL-15^{Med}	3.7 ^{<Mod,Sev} (2, 6)	93.4 ^{>HC} (57, 182)	92.6 ^{>HC} (51, 181)
IL-20^{Med}	42.4 ^{<Mod,Sev} (42, 42)	42.4 ^{>HC} (42, 42)	42.4 ^{>HC} (42, 42)
IL-21^{GM}	3.5x10 ^{2<Mod,Sev} (1.5x10 ² , 1.2x10 ³)	5.5x10 ^{3>HC} (4.4x10 ³ , 6.8x10 ³)	5.6x10 ^{3>HC} (4.4x10 ³ , 7.2x10 ³)
IL-23^{Med}	1.5x10 ^{1<Mod,Sev} (1.5x10 ¹ , 6.9x10 ¹)	5.9x10 ^{2>HC} (9.6x10 ¹ , 1.4x10 ³)	2.7x10 ^{2>HC} (1.0x10 ² , 1.5x10 ³)
IL-25^{Med}	8.2x10 ^{1<Mod,Sev} (8.2x10 ¹ , 5.8x10 ²)	7.4x10 ^{3>HC} (4.3x10 ³ , 1.5x10 ⁴)	8.3x10 ^{3>HC} (4.7x10 ³ , 1.5x10 ⁴)
IL-33^{GM}	9.2 ^{<Mod,Sev} (6, 14)	42.4 ^{>HC} (34, 51)	50.9 ^{>HC} (42, 62)
IL-37^{Med}	44.2 ^{<Mod,Sev} (44, 44)	865.9 ^{>HC} (68, 1572)	801.1 ^{>HC} (305, 1645)
ITAC^{GM}	38.5 ^{<Mod,Sev} (30, 49)	104.1 ^{>HC} (91, 119)	120.4 ^{>HC} (102, 142)
LAP-TGFβ^M	1.5x10 ^{5<Mod,Sev} (1.4x10 ⁵ , 1.7x10 ⁵)	3.2x10 ^{5>HC} (3.1x10 ⁵ , 3.4x10 ⁵)	3.2x10 ^{5>HC} (3.1x10 ⁵ , 3.4x10 ⁵)
LIF^{Med}	4.8 ^{<Mod,Sev} (5, 5)	4.8 ^{>HC} (5, 5)	4.8 ^{>HC} (5, 5)
MCP-1^{GM}	79.1 ^{<Mod,Sev} (68, 92)	191.1 ^{>HC} (179, 204)	201.7 ^{>HC} (187, 218)
MCP-2^{Med}	36.5 ^{<Mod,Sev} (29, 44)	46.6 ^{>HC} (36, 57)	48.4 ^{>HC} (38, 61)
MIG^{GM}	97.2 ^{<Sev} (90, 105)	119.7 (101, 142)	142.6 ^{>HC} (124, 165)
MIP-1β^{Med}	41.0 ^{<Mod,Sev} (33, 51)	122.7 ^{>HC} (110, 137)	124.8 ^{>HC} (113, 138)
MPIF^{Med}	94.4 ^{<Mod,Sev} (41, 171)	371.9 ^{>HC} (199, 530)	404.3 ^{>HC} (246, 562)
Osteopetgrin^{Med}	7.6 ^{<Mod,Sev} (8, 8)	2109.0 ^{>HC} (1656, 2683)	2278.0 ^{>HC} (1888, 2850)
Oncostatin M^{Med}	3.3 ^{<Mod,Sev} (3, 3)	7 ^{>HC} (3, 28)	15 ^{>HC} (3, 43)
%Neutralisation of α-toxin-induced lysis^{Med}	10.8 ^{<Mod,Sev} (1, 21)	26.4 ^{>HC} (15, 56)	35.5 ^{>HC} (23, 80)
S100A8^{Med}	1.2x10 ^{4<Mod,Sev} (8.4x10 ³ , 1.6x10 ⁴)	1.5x10 ^{5>HC} (1.3x10 ⁵ , 1.7x10 ⁵)	1.5x10 ^{5>HC} (1.2x10 ⁵ , 1.7x10 ⁵)
SAA1^{Med}	1.0x10 ^{8<Mod,Sev} (5.2x10 ⁷ , 1.0x10 ⁸)	1.0x10 ^{8>HC} (1.0x10 ⁸ , 1.0x10 ⁸)	1.0x10 ^{8>HC} (1.0x10 ⁸ , 1.0x10 ⁸)
SLPI^{Med}	6.4x10 ^{3<Mod,Sev} (5.9x10 ³ , 7.2x10 ³)	1.9x10 ^{4>HC} (8.7x10 ³ , 1.9x10 ⁴)	1.9x10 ^{4>HC} (9.1x10 ³ , 1.9x10 ⁴)
sSCFR^{Med}	4.2x10 ^{4<Mod,Sev} (3.8x10 ⁴ , 4.4x10 ⁴)	6.3x10 ^{4>HC} (4.9x10 ⁴ , 7.7x10 ⁴)	6.3x10 ^{4>HC} (5.3x10 ⁴ , 7.8x10 ⁴)
TIE-2^{GM}	2.6x10 ^{3<Mod,Sev} (2.3x10 ³ , 2.8x10 ³)	8.6x10 ^{3>HC} (8.1x10 ³ , 9.1x10 ³)	8.6x10 ^{3>HC} (8.1x10 ³ , 9.0x10 ³)
TNFR1^M	5.9x10 ^{2<Mod,Sev} (2.8x10 ² , 9.1x10 ²)	5.6x10 ^{3>HC} (5.2x10 ³ , 5.9x10 ³)	5.7x10 ^{3>HC} (5.3x10 ³ , 6.1x10 ³)
TREM-1^{GM}	1.4x10 ^{1<Mod,Sev} (9.3x10 ⁰ , 2.1x10 ¹)	5.8x10 ^{1>HC} (4.5x10 ¹ , 7.6x10 ¹)	6.6x10 ^{1>HC} (5.4x10 ¹ , 8.2x10 ¹)
TSLP^{GM}	3.3 ^{<Mod,Sev} (2, 7)	15.1 ^{>HC} (12, 18)	17.0 ^{>HC} (14, 21)
VEGF^{Med}	346.4 ^{<Mod,Sev} (170, 603)	685.1 ^{>HC} (372, 1085)	856.5 ^{>HC} (500, 1324)

Variable types are shown in superscript next to variable name; M (mean) for normally distributed data, Med (median) for log-non normally distributed data, GM (geometric mean) for log-normally distributed data. Numbers shown in brackets after measure of central tendency are 95% confidence intervals (for

mean and geomean) or interquartile range (median). Superscript numbers after measure of central tendency are groups that are significantly different.

Table S2. Summary of serum mediators that are differentially upregulated in healthy controls versus atopic dermatitis.

Variables where HC > AD	Healthy controls (n=30)	Moderate AD (n=95)	Severe AD (n=98)
ACE ^{GM}	4.0x10 ^{5>Mod,Sev} (3.6 x10 ⁵ , 4.3 x10 ⁵)	2.8x10 ^{5<HC} (2.6x10 ⁵ , 3.1x10 ⁵)	3.0x10 ^{5<HC} (2.7x10 ⁵ , 3.3x10 ⁵)
Ang2 ^{Med}	1.9x10 ^{4>Mod,Sev} (1.8x10 ⁴ , 2.8x10 ⁴)	1.3x10 ^{4<HC} (1.1x10 ⁴ , 1.5x10 ⁴)	1.4x10 ^{4<HC} (1.2x10 ⁴ , 1.5x10 ⁴)
BDNF ^M	5.5x10 ^{5>Mod,Sev} (4.7x10 ⁵ , 6.2x10 ⁵)	2.2x10 ^{5<HC} (2.1x10 ⁵ , 2.4x10 ⁵)	2.3x10 ^{5<HC} (2.2x10 ⁵ , 2.4x10 ⁵)
Cathepsin S ^M	1.7x10 ^{4>Mod,Sev} (1.6x10 ⁴ , 1.9x10 ⁴)	1.3x10 ^{4<HC} (1.1x10 ⁴ , 1.6x10 ⁴)	1.4x10 ^{4<HC} (1.2x10 ⁴ , 1.7x10 ⁴)
Chemerin 4 ^{Med}	1.9x10 ^{4>Mod,Sev} (1.7x10 ⁴ , 2.5x10 ⁴)	6.8x10 ^{3<HC} (6.8x10 ³ , 2.1x10 ⁴)	1.4x10 ^{4<HC} (6.8x10 ³ , 2.2x10 ⁴)
EGF ^{GM}	24.3 ^{>Mod,Sev} (12, 49)	13.8 ^{<HC} (12, 16)	15.5 ^{<HC} (14, 18)
Galectin-3 ^{GM}	2.8x10 ^{4>Mod,Sev} (2.6x10 ⁴ , 3.0x10 ⁴)	2.0x10 ^{4<HC} (1.8x10 ⁴ , 2.1x10 ⁴)	2.1x10 ^{4<HC} (2.0x10 ⁴ , 2.3x10 ⁴)
Galectin-9 ^{Med}	3.2x10 ^{3>Mod,Sev} (2.3x10 ³ , 4.4x10 ³)	1.0x10 ^{1<HC} (1.0x10 ¹ , 8.1x10 ³)	1.0x10 ^{1<HC} (1.0x10 ¹ , 1.0x10 ¹)
IFN-β ^{Med}	3.2x10 ^{2>Mod,Sev} (1.5x10 ² , 9.1x10 ²)	1.4x10 ^{2<HC} (9.7x10 ⁰ , 3.4x10 ²)	1.4x10 ^{2<HC} (9.7x10 ⁰ , 2.8x10 ²)
IL-27 ^{Med}	1.4x10 ^{3>Mod,Sev} (4.7x10 ² , 2.7x10 ³)	1.6x10 ^{0<HC} (1.6x10 ⁰ , 1.9x10 ⁴)	1.6x10 ^{0<HC} (1.6x10 ⁰ , 1.6x10 ⁰)
Leptin-3 ^{Med}	3.6x10 ^{3>Mod,Sev} (2.8x10 ³ , 5.4x10 ³)	8.0x10 ^{2<HC} (8.0x10 ² , 1.9x10 ³)	8.0x10 ^{2<HC} (8.0x10 ² , 2.0x10 ³)
MIF ^{GM}	7.0x10 ^{3>Mod,Sev} (5.2x10 ³ , 9.3x10 ³)	2.8x10 ^{3<HC} (2.5x10 ³ , 3.1x10 ³)	3.2x10 ^{3<HC} (2.8x10 ³ , 3.6x10 ³)
PAI-1 ^{Med}	9.5x10 ^{5>Mod,Sev} (6.6x10 ⁵ , 1.3x10 ⁶)	6.9x10 ^{5<HC} (2.9x10 ⁵ , 9.6x10 ⁵)	7.5x10 ^{5<HC} (1.7x10 ⁵ , 1.0x10 ⁶)
P-selectin ^{Med}	5.5x10 ^{5>Mod,Sev} (3.5x10 ⁵ , 1.4x10 ⁶)	3.4x10 ^{5<HC} (2.0x10 ⁵ , 5.5x10 ⁵)	3.7x10 ^{5<HC} (2.2x10 ⁵ , 6.6x10 ⁵)
RBP-4 ^{Med}	2.8x10 ^{7>Mod,Sev} (2.7x10 ⁷ , 2.9x10 ⁷)	2.6x10 ^{7<HC} (2.4x10 ⁷ , 2.9x10 ⁷)	2.6x10 ^{7<HC} (2.4x10 ⁷ , 2.8x10 ⁷)
Resistin ^{Med}	9.4x10 ^{3>Mod,Sev} (8.9x10 ³ , 1.0x10 ⁴)	6.8x10 ^{3<HC} (5.7x10 ³ , 9.3x10 ³)	7.5x10 ^{3<HC} (6.0x10 ³ , 9.5x10 ³)
sCD14 ^{Med}	2.3x10 ^{6>Mod,Sev} (2.1x10 ⁶ , 2.5x10 ⁶)	1.3x10 ^{6<HC} (1.1x10 ⁶ , 1.8x10 ⁶)	1.5x10 ^{6<HC} (1.2x10 ⁶ , 2.0x10 ⁶)
sCD163 ^{Med}	1.4x10 ^{5>Mod,Sev} (1.2x10 ⁵ , 1.7x10 ⁵)	4.3x10 ^{4<HC} (4.3x10 ⁴ , 4.3x10 ⁴)	4.3x10 ^{4<HC} (4.3x10 ⁴ , 4.3x10 ⁴)
SCF ^{Med}	50.8 ^{>Mod,Sev} (38, 59)	31.5 ^{<HC} (20, 45)	34.5 ^{<HC} (21, 52)
siL-2Rα ^{Med}	23.5 ^{>Mod,Sev} (24, 336)	23.5 ^{<HC} (24, 24)	23.5 ^{<HC} (24, 24)
TACI ^{Med}	8.9x10 ^{4>Mod,Sev} (6.6x10 ⁴ , 1.1x10 ⁵)	8.0x10 ^{2<HC} (8.0x10 ² , 8.0x10 ²)	8.0x10 ^{2<HC} (8.0x10 ² , 8.0x10 ²)
TECK ^{Med}	915.9 ^{>Mod,Sev} (562, 1324)	405.0 ^{<HC} (294, 601)	481.3 ^{<HC} (306, 755)
TPO ^{Med}	8.6x10 ^{6>Mod,Sev} (8.0x10 ⁶ , 9.1x10 ⁶)	9.2x10 ^{5<HC} (7.2x10 ⁵ , 1.2x10 ⁶)	9.7x10 ^{5<HC} (7.6x10 ⁵ , 1.3x10 ⁶)
Trappin-2 ^{Med}	2226.0 ^{>Mod,Sev} (1924, 2576)	123.1 ^{<HC} (27, 243)	99.8 ^{<HC} (29, 240)

TWEAK ^{GM}	1.6x10 ^{4>Mod,Sev} (1.4x10 ⁴ , 1.9x10 ⁴)	9.9x10 ^{3<HC} (9.3x10 ³ , 1.1x10 ⁴)	1.0x10 ^{4<HC} (9.3x10 ³ , 1.1x10 ⁴)
VCAM-1 ^{Med}	4.3x10 ^{6>Mod,Sev} (3.7x10 ⁶ , 5.3x10 ⁶)	2.0x10 ^{6<HC} (1.6x10 ⁶ , 2.5x10 ⁶)	2.2x10 ^{6<HC} (1.8x10 ⁶ , 2.6x10 ⁶)

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