

	Number	Sex		Age (mnths)		Age AD onset (wks)		SCORAD		TEWL		<i>FLG</i> status			
		male	female	average	range	average	range	average	range	average	range	WT	HET	HOM	unknown
Plasma AD patients	47	34	13	6.7	0-11	11.8	2-44	48	25-91.3	26	8.5-53.9	26	18	3	1
SC AD patients	66	49	17	7	0-11	11	2-44	45.2	25-85	24.1	8.3-53.9	30	27	5	4
Plasma controls	20	14	6	6.5	0-12	-	-	-	-	11	4-15.6	18	2	0	0
SC controls	13	9	4	6.7	0-12	-	-	-	-	12	8.1-15.6	11	2	0	0

Table 6.1: Patient demographics, SCORAD, TEWL and *FLG* status

	CTRL (n = 13) <i>median(range)</i>	AD (n = 66) <i>median(range)</i>	Ctrl vs. AD (adjusted <i>p</i> - value)	CTRL (n = 20) <i>median(range)</i>	AD (n = 47) <i>median(range)</i>	Ctrl vs. AD (adjusted <i>p</i> - value)
Fit-1	-1,812(-2,699 to -1,449)	-1,095(-1,684 to -0,195)	< 0.0001 ⁽¹⁾	1,460(-0,387 to 1,648)	1,530(0,524 to 1,810)	0.1371
Tie-2	-1,234(-1,588 to -0,452)	-1,204(-2,721 to -0,539)	0.9162	3,735(2,493 to 3,834)	3,892(2,794 to 4,160)	< 0.0001
VEGF-A	-0,864(-2,108 to -0,552)	-0,637(-2,071 to -0,010)	0.0200	1,488(0,961 to 2,048)	1,578(0,649 to 2,227)	0.9332 ⁽¹⁾
VEGF-C			< DL	1,725(0,513 to 2,092)	2,135(1,650 to 2,554)	< 0.0001
CCL2 (MCP-1)	-2,208(-3,155 to -1,917)	-1,845(-3,222 to -0,821)	0.0055 ⁽¹⁾	2,269(1,913 to 2,527)	2,208(1,655 to 2,627)	0.2641 ⁽¹⁾
CCL22 (MDC)	-0,425(-0,555 to -0,306)	0,046(-0,577 to 0,785)	< 0.0001 ⁽¹⁾	3,406(2,717 to 3,781)	3,606(2,588 to 4,256)	0.0071
CCL17 (TARC)	-1,580(-1,947 to -1,409)	-1,221(-1,876 to 0,051)	0.0007	2,103(1,661 to 3,159)	2,750(2,189 to 3,894)	< 0.0001
IL-5	-1,699(-1,959 to -1,491)	-1,863(-2,444 to -1,350)	0.0022 ⁽¹⁾	-0,124(-0,588 to 0,200)	0,176(-0,263 to 1,428)	< 0.0001
IL-13	-1,154(-1,381 to -1,035)	-1,320(-1,839 to -0,847)	0.0052 ⁽¹⁾	-1,331(-1,331 to 0,509)	-0,115(-1,331 to 0,500)	0.0133
IL-1α	1,252(0,820 to 1,662)	0,805(-0,731 to 1,730)	0.0022			< DL
IL-18	-1,606(-2,310 to -1,271)	-0,063(-1,536 to 1,817)	< 0.0001 ⁽¹⁾	3,160(2,887 to 3,717)	3,334(2,113 to 3,692)	0.1906
IL-1β	-1,767(-2,187 to -1,102)	-1,395(-2,328 to -0,571)	0.0097 ⁽¹⁾	-1,080(-2,770 to 0,294)	-1,340(-2,770 to -0,164)	0.3598
CXCL8 (IL-8)	-2,060(-2,357 to -1,541)	-1,185(-2,187 to 0,794)	< 0.0001	1,036(0,550 to 2,662)	1,113(0,367 to 1,983)	0.6895
CXCL10 (IP-10)	-2,721(-4,000 to -1,851)	-2,310(-4,000 to -0,418)	0.0785	2,513(2,050 to 3,223)	2,263(0,898 to 3,268)	0.0097
CCL13 (MCP-4)	-0,564(-0,798 to -0,377)	-0,601(-1,214 to -0,255)	0.3598 ⁽¹⁾	2,406(2,073 to 2,657)	2,685(1,425 to 3,795)	0.0005
CCL3 (MIP-1α)	-0,761(-1,078 to -0,578)	-0,890(-1,710 to -0,369)	0.1473	1,400(0,339 to 1,665)	1,336(0,339 to 1,964)	0.2779
CCL4 (MIP-1β)	-0,310(-0,442 to -0,084)	-0,490(-0,881 to -0,014)	< 0.0001 ⁽¹⁾	1,957(1,526 to 2,158)	1,814(1,267 to 2,343)	0.1507 ⁽¹⁾
GM-CSF	-1,857(-2,114 to -0,789)	-2,194(-2,854 to -1,686)	0.0002	-0,647(-1,928 to -0,082)	-0,217(-2,143 to 0,576)	0.0010
IL-7	-1,928(-2,824 to -1,578)	-1,971(-3,046 to -1,654)	0.4594	0,906 (0,617 to 1,189)	0,952(0,168 to 1,427)	0.5034 ⁽¹⁾
IL-12p40	-1,095(-1,463 to 0,005)	-1,303(-2,167 to -0,279)	0.0107	2,723(2,293 to 2,972)	2,578(0,477 to 3,237)	0.0531 ⁽¹⁾
IL-15	-2,081(-2,886 to -0,943)	-2,523(-3,523 to -1,824)	0.0121 ⁽¹⁾	0,169(-0,032 to 0,404)	0,045(-0,743 to 0,444)	0.0515
IL-16	-1,324(-1,924 to -1,042)	-1,151(-1,728 to -0,311)	0.0160 ⁽¹⁾	2,814(2,340 to 3,151)	2,912(2,109 to 3,855)	0.1902 ⁽¹⁾
IL-17A	-1,499(-2,119 to -1,249)	-1,439(-2,886 to -0,874)	0.4940	0,909(0,491 to 1,881)	0,940(0,123 to 2,059)	0.6916
IL-2	-1,975(-2,174 to -1,818)	-2,081(-2,658 to -1,252)	0.1748	-0,656(-2,161 to 0,089)	-0,666(-2,161 to 0,367)	0.8061
CRP	0,535(0,083 to 0,938)	0,743(-0,244 to 1,753)	0.0552 ⁽¹⁾	5,939(2,790 to 7,740)	5,376(2,489 to 7,745)	0.1402
SAA	1,303(1,058 to 1,489)	1,390(0,967 to 2,102)	0.0074 ⁽¹⁾	6,065(4,646 to 8,464)	5,879(4,329 to 8,113)	0.4609
sICAM-1	0,363(0,276 to 0,619)	0,729(0,176 to 1,478)	< 0.0001 ⁽¹⁾	5,859(2,821 to 5,956)	5,835(3,605 to 6,107)	0.6295
sVCAM-1	0,573(0,368 to 0,770)	0,768(0,170 to 1,501)	0.0004 ⁽¹⁾	5,911(3,657 to 6,208)	5,939(3,676 to 6,268)	0.4438

¹two-tailed Welch *t*-test (otherwise two-tailed Mann-Whitney test)

nd → not determined in the SC

< DL → more than 50 % of values bellow fit curve range

adjusted *p*-values → BH corrected *p*-values

Angiogenesis markers

Th2 skewed markers

Markers of innate activation

Others

Table 6.2. Continued....

	SC			Plasma		
	CTRL (<i>n</i> = 13) <i>median</i> (range)	AD (<i>n</i> = 66) <i>median</i> (range)	Ctrl vs. AD (adjusted <i>p</i> -value)	CTRL (<i>n</i> = 20) <i>median</i> (range)	AD (<i>n</i> = 47) <i>median</i> (range)	Ctrl vs. AD (adjusted <i>p</i> -value)
PIGF				1,048(-0,091 to 1,221)	1,111(0,211 to 1,417)	0.0202
VEGF-D				2,817(2,362 to 3,055)	2,841(2,221 to 3,111)	0.4998
CCL26 (Eotaxin-3)				2,147(1,638 to 2,548)	2,479(1,178 to 3,709)	0.0002
CCL11 (Eotaxin)				2,637(2,294 to 2,887)	2,538(1,132 to 2,905)	0.4261
IL-4				-4,000(-4,000 to -0,245)	-2,222(-4,000 to 0,140)	0.0072
CCL5 (RANTES)		nd		4,427(1,230 to 5,662)	4,657(1,230 to 5,524)	0.1608
TNF-β				-0,126(-0,416 to 0,204)	-0,154(-1,507 to 0,579)	0.7144
TNF-α				0,905(0,526 to 1,289)	0,925(0,121 to 1,293)	0.7693
bFGF				0,991(-0,523 to 1,813)	0,760(-0,222 to 1,605)	0.0936
IFN-γ				1,155(0,246 to 1,991)	1,098(-0,086 to 2,473)	0.4998
IL-6				-0,015(-2,745 to 0,448)	-0,194(-2,745 to 0,798)	0.2641
IL-10				0,126(-0,466 to 0,997)	0,095(-0,858 to 0,743)	0.4261 ⁽¹⁾

¹two-tailed Welch *t*-test (otherwise two-tailed Mann-Whitney test)

nd → not determined in the SC

< DL → more than 50 % of values bellow fit curve range

adjusted *p*-values → BH corrected *p*-values

Angiogenesis markers	Th2 skewed markers	Markers of innate activation	Others
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Table 6.2 Study raw data

Cytokine and chemokine levels (log-transformed values) and differences between their levels in the SC and plasma of healthy control children (CTRL) and children with AD (AD).

logCYT	oSCORAD						SCORAD					
	SC (n = 66)			Plasma (n = 47)			SC (n = 66)			Plasma (n = 47)		
	r	Adjusted p-value	95 % C.I.	r	Adjusted p-value	95 % C.I.	r	Adjusted p-value	95 % C.I.	r	Adjusted p-value	95 % C.I.
Flt-1	0,4303	0,0019	0,2031 to 0,6135	-0,0142	0,9413	-0,3081 to 0,2822	0,4141	0,0028	0,1841 to 0,6011	0,0638	0,7692	-0,2358 to 0,5
Tie-2	-0,1530	0,2384	-0,3810 to 0,0925	-0,1779	0,3598	-0,4495 to 0,1239	0,2553	0,0976	0,0068 to 0,4741	-0,1841	0,3456	-0,4546 to 0,1
VEGF-A	0,4427	0,0014	0,2177 to 0,6230	0,0371	0,8719	-0,2642 to 0,3318	0,4496	0,0012	0,2259 to 0,6282	0,0635	0,7692	-0,2394 to 0,5
VEGF-C		< DL		-0,0349	0,8719	-0,3267 to 0,2630		< DL		-0,0545	0,8049	-0,3442 to 0,2
CCL2 (MCP-1)	0,4076	0,0034	0,1767 to 0,5960	0,0312	0,8897	-0,2697 to 0,3265	0,3983	0,0044	0,1658 to 0,5889	0,0911	0,6709	-0,2131 to 0,5
CCL22 (MDC)	0,3625	0,0107	0,1249 to 0,5608	0,4888	0,0028	0,2229 to 0,6870	0,3730	0,0086	0,1368 to 0,5691	0,3968	0,0202	0,1116 to 0,6
CCL17 (TARC)	0,4356	0,0017	0,2093 to 0,6176	0,3596	0,0425	0,0685 to 0,5943	0,4136	0,0028	0,1836 to 0,6007	0,3204	0,0788	0,0242 to 0,5
IL-5	-0,2169	0,3181	-0,4361 to 0,0266	0,4101	0,0160	0,1272 to 0,6313	-0,1104	0,5063	-0,3498 to 0,1424	0,4107	0,0160	0,1280 to 0,6
IL-13	0,2300	0,1474	-0,0221 to 0,4546	0,2038	0,2934	-0,1008 to 0,4734	0,1901	0,2424	-0,0638 to 0,4209	0,2242	0,2474	-0,0796 to 0,4
IL-1α	-0,2685	0,0785	-0,4850 to -0,0209		< DL		-0,1892	0,2424	-0,4185 to 0,0627		< DL	
IL-18	0,4221	0,0022	0,1936 to 0,6072	0,2985	0,1072	4,895e-005 to 0,5481	0,3704	0,0090	0,1338 to 0,5671	0,3028	0,1015	0,0048 to 0,5
IL-1β	0,1307	0,4376	-0,1242 to 0,3694	0,2134	0,2718	-0,0908 to 0,4812	0,2008	0,2183	-0,0527 to 0,4300	0,2087	0,2806	-0,0957 to 0,4
CXCL8 (IL-8)	0,5338	< 0,0001	0,3267 to 0,6920	0,4112	0,0160	0,1287 to 0,6321	0,4609	0,0009	0,2375 to 0,6380	0,4118	0,0487	0,1379 to 0,6
CXCL10 (IP-10)	0,1094	0,5096	-0,1434 to 0,3489	-0,0206	0,9261	-0,3171 to 0,2796	0,0868	0,6214	-0,1657 to 0,3286	-0,0169	0,9332	-0,3138 to 0,2
CCL13 (MCP-4)	0,0522	0,7693	-0,1992 to 0,2972	0,4045	0,0177	0,1206 to 0,6272	0,0553	0,7633	-0,1963 to 0,3001	0,3649	0,0385	0,0746 to 0,5
CCL3 (MIP-1α)	-0,1796	0,2641	-0,4102 to 0,0726	0,4027	0,0183	0,1185 to 0,6259	-0,1707	0,2887	-0,4026 to 0,08168	0,3211	0,0785	0,0251 to 0,5
CCL4 (MIP-1β)	-0,0335	0,8593	-0,2800 to 0,2172	0,1605	0,4261	-0,1448 to 0,4379	-0,0138	0,9332	-0,2618 to 0,2360	0,1467	0,4665	-0,1586 to 0,4
GM-CSF	0,0193	0,9218	-0,2307 to 0,2669	0,1387	0,4951	-0,1667 to 0,4197	0,0800	0,6503	-0,1724 to 0,3225	0,1174	0,5666	-0,1876 to 0,4
IL-7	-0,0721	0,6834	-0,3154 to 0,1801	0,2084	0,2806	-0,0960 to 0,4771	-0,0018	0,9888	-0,2506 to 0,2473	0,1911	0,3298	-0,1137 to 0,4
IL-12p40	0,1395	0,3997	-0,1134 to 0,3754	0,2013	0,4694	-0,0981 to 0,4673	0,1827	0,2601	-0,0694 to 0,4129	0,1759	0,5329	-0,1241 to 0,4
IL-15	-0,1511	0,3581	-0,3855 to 0,1016	0,1042	0,6215	-0,2005 to 0,3905	-0,0994	0,5567	-0,3399 to 0,1534	0,1349	0,5033	-0,1704 to 0,4
IL-16	0,3079	0,0373	0,0639 to 0,5172	0,2722	0,1494	-0,0285 to 0,5277	0,3189	0,0285	0,0760 to 0,5261	0,1779	0,3648	-0,1272 to 0,4
IL-17A	0,1642	0,3100	-0,0883 to 0,3970	0,3021	0,0979	0,0077 to 0,5484	0,1910	0,2394	-0,0609 to 0,4199	0,2972	0,1046	0,0023 to 0,5
IL-2	0,1029	0,5379	-0,1499 to 0,3431	0,0498	0,8178	-0,2524 to 0,3431	0,0736	0,6800	-0,1786 to 0,3167	0,0731	0,7321	-0,2304 to 0,5
CRP	0,2019	0,2161	-0,0516 to 0,4308	0,1580	0,4261	-0,1439 to 0,4331	0,1697	0,2952	-0,0848 to 0,4034	0,1688	0,3906	-0,1330 to 0,4
SAA	0,4517	0,0012	0,2266 to 0,6310	0,2148	0,2641	-0,0858 to 0,4796	0,4328	0,0019	0,2041 to 0,6167	0,2105	0,2720	-0,0904 to 0,4
sICAM-1	0,4781	0,0005	0,2583 to 0,6509	-0,0650	0,7692	-0,3565 to 0,2380	0,4623	0,0009	0,2392 to 0,6391	-0,1135	0,5805	-0,3984 to 0,1
sVCAM-1	0,4391	0,0017	0,2116 to 0,6215	0,3724	0,0337	0,0832 to 0,6037	0,4420	0,0016	0,2150 to 0,6237	0,3107	0,0927	0,0136 to 0,5

nd → not determined in the SC

< DL → more than 50 % of values bellow fit curve range

adjusted p-values → BH corrected p-values

Table 6.3 Continued.....

Angiogenesis markers Th2 skewed markers Markers of innate activation Others

logCYT	oSCORAD						SCORAD					
	SC (n = 66)			Plasma (n = 47)			SC (n = 66)			Plasma (n = 47)		
	r	Adjusted p-value	95 % C.I.	r	Adjusted p-value	95 % C.I.	r	Adjusted p-value	95 % C.I.	r	Adjusted p-value	95 % C.I.
PIGF				-0,1248	0,5376	-0,4080 to 0,1804				-0,0940	0,6582	-0,3817 to 0,1927
VEGF-D				0,0352	0,8719	-0,2627 to 0,3270				0,0211	0,9261	-0,2759 to 0,2281
CCL26 (Eotaxin-3)				0,3314	0,0646	0,0401 to 0,5708				0,4220	0,0119	0,1448 to 0,6992
CCL11 (Eotaxin)				0,1561	0,4376	-0,1493 to 0,4343				0,1131	0,5805	-0,1918 to 0,4081
IL-4				-0,0756	0,7231	-0,3627 to 0,2247				-0,0350	0,8719	-0,3268 to 0,2568
CCL5 (RANTES)		nd		-0,0169	0,9332	-0,3106 to 0,2797		nd		-0,0207	0,9269	-0,3140 to 0,2666
TNF-β				-0,0027	0,9505	-0,3009 to 0,2960				-0,0150	0,9088	-0,3120 to 0,2820
TNF-α				0,5008	0,0020	0,2413 to 0,6935				0,4039	0,0165	0,1234 to 0,6844
bFGF				-0,0829	0,6916	-0,3691 to 0,2176				-0,1121	0,5805	-0,3942 to 0,1699
IFN-γ				0,2679	0,1507	-0,0297 to 0,5219				0,2844	0,1252	-0,0118 to 0,5219
IL-6				0,2799	0,1325	-0,0167 to 0,5312				0,2904	0,1152	-0,0052 to 0,5219
IL-10				0,2636	0,1578	0,0342 to 0,5185				0,1930	0,3180	-0,1083 to 0,4523

nd → not determined in the SC

< DL → more than 50 % of values bellow fit curve range

adjusted p-values → BH corrected p-values

Angiogenesis markers Th2 skewed markers Markers of innate activation Others

Table 6.3 Study raw data

Correlation (two-tailed Spearman's test) between cytokines/chemokines (log-transformed values) and oSCORAD/ SCORAD in the SC and in plasma of children with AD.

logCYT	TEWL					
	SC (n = 66)			Plasma (n = 47)		
	r	Adjusted p-value	95 % C.I.	r	Adjusted p-value	95 % C.I.
FIt-1	0,6716	< 0,0001	0,5060 to 0,7895	-0,1539	0,4438	-0,4325 to 0,1515
Tie-2	0,2270	0,1507	-0,0253 to 0,4521	-0,2276	0,2424	-0,4926 to 0,0760
VEGF-A	0,5624	< 0,0001	0,3627 to 0,7127	-0,0980	0,6503	-0,3883 to 0,2099
VEGF-C		< DL		0,0754	0,7254	-0,2281 to 0,3656
CCL2 (MCP-1)	0,2598	0,0936	0,0096 to 0,4794	0,1927	0,3302	-0,1158 to 0,4673
CCL22 (MDC)	0,4374	0,0017	0,2095 to 0,6202	0,5639	0,0005	0,3159 to 0,7398
CCL17 (TARC)	0,4910	0,0004	0,2739 to 0,6605	0,5981	0,0002	0,3616 to 0,7623
IL-5	-0,2462	0,1152	-0,4682 to 0,0049	0,2590	0,1789	-0,0464 to 0,5201
IL-13	0,0116	0,9414	-0,2419 to 0,2637	0,2337	0,2384	-0,0732 to 0,5002
IL-1α	-0,3735	0,0090	-0,5709 to -0,1353		< DL	
IL-18	0,7340	< 0,0001	0,5922 to 0,8317	0,3278	0,0765	0,0289 to 0,5729
IL-1β	0,1142	0,5022	-0,1427 to 0,3568	0,1502	0,4609	-0,1588 to 0,4323
CXCL8 (IL-8)	0,5763	< 0,0001	0,3786 to 0,7237	0,2139	0,2751	-0,0939 to 0,4844
CXCL10 (IP-10)	0,2403	0,1269	-0,0113 to 0,4632	0,0049	0,9779	-0,2973 to 0,3062
CCL13 (MCP-4)	0,0449	0,8061	-0,2084 to 0,2924	0,5216	0,0016	0,2609 to 0,7114
CCL3 (MIP-1α)	-0,2165	0,1748	-0,4433 to 0,03631	0,2342	0,2384	-0,0726 to 0,5006
CCL4 (MIP-1β)	-0,2729	0,0765	-0,4902 to -0,0237	0,2214	0,2616	-0,0861 to 0,4904
GM-CSF	-0,1899	0,2424	-0,4207 to 0,0640	0,4192	0,0152	0,1345 to 0,6400
IL-7	-0,1529	0,3573	-0,3888 to 0,1019	0,1659	0,4157	-0,1430 to 0,4454
IL-12p40	0,0052	0,9741	-0,2459 to 0,2558	0,2424	0,3876	-0,0677 to 0,5099
IL-15	-0,1885	0,2463	-0,4195 to 0,0655	0,0875	0,6837	-0,2201 to 0,3792
IL-16	0,2954	0,0498	0,0481 to 0,5086	0,5299	0,0013	0,2716 to 0,7170
IL-17A	0,1688	0,2974	-0,0857 to 0,4026	0,4753	0,0041	0,2061 to 0,6776
IL-2	0,0379	0,8350	-0,2150 to 0,2861	-0,0756	0,7254	-0,3690 to 0,2314
CRP	0,1941	0,2394	-0,0617 to 0,4261	0,1036	0,6220	-0,2011 to 0,3899
SAA	0,2813	0,0678	0,0307 to 0,4987	0,0481	0,8238	-0,2540 to 0,3416
sICAM-1	0,4206	0,0028	0,1878 to 0,6087	-0,1469	0,4694	-0,4296 to 0,1620
sVCAM-1	0,3905	0,0064	0,1528 to 0,5856	0,2570	0,1827	-0,0485 to 0,5185

nd → not determined in the SC

< DL → more than 50 % of values bellow fit curve range

adjusted p-values → BH corrected p-values

Angiogenesis markers Th2 skewed markers Markers of innate activation Others

Table 6.4. Continued....

logCYT	TEWL					
	SC (n = 66)			Plasma (n = 47)		
	r	Adjusted p-value	95 % C.I.	r	Adjusted p-value	95 % C.I.
PIGF				-0,0892	0,6810	-0,3807 to 0,2185
VEGF-D				0,1264	0,5329	-0,1787 to 0,4094
CCL26 (Eotaxin-3)				0,4103	0,0160	0,1275 to 0,6315
CCL11 (Eotaxin)				0,5146	0,0018	0,2520 to 0,7066
IL-4				0,0511	0,8141	-0,2512 to 0,3443
CCL5 (RANTES)		nd		-0,0527	0,8087	-0,3457 to 0,2497
TNF-β				0,3303	0,1494	0,0317 to 0,5748
TNF-α				0,1796	0,3598	-0,1256 to 0,4537
bFGF				-0,0956	0,6528	-0,3831 to 0,2088
IFN-γ				0,0552	0,8049	-0,2473 to 0,3479
IL-6				0,0350	0,8719	-0,2662 to 0,3300
IL-10				0,2390	0,2185	-0,0640 to 0,5017

nd → not determined in the SC

< DL → more than 50 % of values bellow fit curve range

adjusted p-values → BH corrected p-values

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Table 6.4 Study raw data

Correlation (two-tailed Spearman's test) between cytokines/chemokines (log-transformed values) and TEWL in the SC and in plasma of children with AD.