

EASI p-EASI: Utilising a combination of serum biomarkers offers an objective measurement tool for disease severity in atopic dermatitis patients

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Table S1. Correlation coefficients of SASSAD with serum biomarkers in the retrospective cohort.

biomarker	r	p-value	biomarker	r	p-value
IL-1ra	-0.19	0.03	EGF	0.05	0.62
IL-1a	-0.10	0.28	FGFb	-0.17	0.07
IL-1b	0.04	0.71	NGF	-0.13	0.17
IL-2	-0.13	0.19	PLGF	-0.04	0.72
IL-3	-0.04	0.71	VEGF	0.22	0.01
IL-4	-0.09	0.34	MMP-9	0.04	0.72
IL-5	0.03	0.80	Trem-1	-0.09	0.34
IL-6	-0.14	0.16	Cathepsin-b	0.05	0.60
IL-7	0.02	0.81	PD-1	-0.10	0.28
IL-9	-0.03	0.79	FAS	0.14	0.15
IL-10	-0.25	0.00	FAS ligand	-0.06	0.57
IL-11	-0.24	0.01	LAIR-1	-0.09	0.34
IL-12	-0.02	0.82	IL-18bpa	0.14	0.16
IL-13	0.02	0.81	IL-1r1	-0.13	0.18
IL-15	-0.03	0.81	IL-1r2	0.10	0.28
IL-16	0.04	0.73	IL-1r4	-0.03	0.80
IL-17	-0.22	0.01	TNFR1	0.12	0.22
IL-18	0.39	0.00	TNFR2	0.25	0.00
IL-109	-0.01	0.89	sIL-2R	0.06	0.60
IL-20	-0.10	0.30	VEGFR1	0.06	0.60
IL-21	-0.09	0.34	SSCFR	0.12	0.19
IL-22	0.24	0.01	EPOR	-0.16	0.09
IL-23	0.02	0.85	Galectin-1	0.06	0.59
IL-25	-0.01	0.93	Galectin-9	-0.17	0.07
IL-26	-0.28	0.00	P-selectin	0.10	0.30
IL-27	-0.14	0.15	E-selectin	0.35	0.00
IL-29	-0.17	0.07	Cystc	0.13	0.17
IL-31	-0.09	0.34	SLPI	-0.15	0.11
IL-33	0.05	0.60	Elastase	0.05	0.67
IL-37	-0.07	0.49	Trappin2	-0.21	0.02
TNF- α	-0.14	0.15	GCP2	-0.11	0.28
TNF- β	-0.11	0.28	Endoglin	0.13	0.17
IFN- α	0.16	0.10	TWEAK	0.19	0.03
IFN- β	-0.22	0.01	SOST	-0.21	0.02
IFN- γ	-0.17	0.07	PF4	0.02	0.85
LIGHT	-0.26	0.00	Apelin	0.08	0.43
MIF	0.10	0.30	TIE2	0.11	0.28
LIF	-0.23	0.01	Ang-1	0.06	0.59
OSM	-0.06	0.60	Ang-2	0.12	0.22
TSLP	-0.04	0.73	DKK1	0.11	0.28
I-309	0.32	0.00	YKL40	0.08	0.41
MCP1	0.08	0.41	TACI	0.09	0.34
Mip1a	0.14	0.16	Ace	0.09	0.34
Mip1b	0.06	0.60	C5a	0.00	0.99

MCP3	-0.13	0.17	Galectin-3	0.04	0.71
MCP2	0.09	0.34	Cathepsin L	0.21	0.02
Eotaxin	-0.02	0.85	Cathepsin S	0.09	0.34
MCP4	0.21	0.02	S100A12	-0.31	0.00
TARC	0.42	0.00	Timp1	0.21	0.02
Mip3b	-0.11	0.28	MMP 1	0.23	0.01
Mip3a	0.11	0.27	MMP 3	0.01	0.89
MDC	0.38	0.00	MMP 8	0.25	0.00
MPIF	0.02	0.81	ICAM	0.18	0.05
Teck	0.01	0.90	VCAM	0.07	0.46
Eotaxin3	-0.04	0.72	BDNF	-0.08	0.42
CTACK	0.13	0.19	SDF-1α	0.30	0.00
Gro-α	-0.01	0.90	tpo	0.28	0.00
ENA78	0.12	0.20	SAA1	-0.10	0.28
IL-8	0.01	0.90	Leptin	0.02	0.82
MIG	0.04	0.71	Chemerin	-0.19	0.03
Ip10	0.17	0.07	Resistin	0.12	0.19
ITAC	0.05	0.60	PAI1	0.25	0.00
BLC	0.06	0.59	RBP4	-0.12	0.22
BRAK	0.11	0.28	Adipsin	-0.16	0.09
SRPSOX	-0.06	0.56	PARC	0.32	0.00
XCL-1	-0.28	0.00	LapTGFβ	-0.15	0.14
OPG	0.09	0.35	GDF15	0.11	0.25
OPN	0.22	0.01	RANTES	0.20	0.03
Kim-1	-0.10	0.31	Adiponectin	-0.04	0.71
GCSF	-0.14	0.15	sCD14	0.14	0.17
MCSF	-0.03	0.81	sCD163	-0.05	0.67
GMCSF	-0.03	0.81	S100A8	-0.13	0.17
SCF	-0.09	0.34	NAP2	0.13	0.17
HGF	0.23	0.01	Total IgE	0.29	0.00

This table shows the Pearson correlation coefficients (r) between SASSAD and serum biomarkers. corrected for multiple testing by adjusting the false discovery rate using the Benjamini-Hochberg procedure.

Table S2. Results linear mixed model analysis for prediction of EASI scores

Effect	Estimate	Standard Error	P value
Baseline			
TARC (per increase of 1 log)	18.4941	2.2787	<.0001
IL-22 (per increase of 1 unit)	0.008942	0.004020	<0.05
sIL-2R (per increase of 1 unit)	-0.00946	0.004050	<0.05
Slope 2 (between t₁ and t₂)			
TARC (per increase of 1 log)	4.0392	5.0026	0.0369
IL-22 (per increase of 1 unit)	0.002739	1.8357	0.3503
sIL-2R (per increase of 1 unit)	-0.00284	0.002879	0.3350

55/65 randomly selected patients were included in the model building. Akaike information criteria were used to identify the best model for the prediction of EASI scores. The best model for EASI changes over time included the biomarkers TARC, IL-22 and sIL-2R. This resulted in the following equations: EASI (before treatment i.e at baseline)= $-36.1180 + 18.4941 * \text{LogTARC} + 0.008942 * \text{IL-22} - 0.00946 * \text{sIL-2R}$; EASI (during treatment)= $-5.8183 + (4.0392 * \text{LogTARC}) + (0.002739 * \text{IL-22}) - (0.00284 * \text{sIL-2R})$. The signature was validated in the remaining 10 AD patients by comparing the predicted EASI scores with the observed EASI scores (Table S3).

Table S3. Validation of the model

Prediction of EASI scores									
Patiënt ID	TARC (pg/ml)	Log TARC (pg/ml)	IL-22 (pg/ml)	sIL-2R (pg/ml)	EASI	severity	predicted EASI	predicted severity	correct prediction
7-0	212.42	2.33	0.02	207.11	0	mild	5.01	mild	yes
7-1	226.88	2.36	0.02	101.47	0	mild	3.43	mild	yes
7-2	186.01	2.27	0.02	170.38	0.5	mild	2.87	mild	yes
11-0	3309.25	3.52	215.71	413.49	16.8	moderate	27.00	severe	no
11-1	783.25	2.89	67.39	201.09	5.05	mild	5.47	mild	yes
11-2	1692.58	3.23	77.9	213.1	3.4	mild	6.84	mild	yes
24-0	359.60	2.56	6.79	113.5	1.2	mild	10.21	moderate	no
24-1	351.28	2.55	0.02	1.61	0.4	mild	4.48	mild	yes
24-2	312.40	2.49	1.62	55.49	0	mild	4.09	mild	yes
25-0	609.92	2.79	6.73	419.98	9.6	moderate	11.57	moderate	yes
25-1	636.02	2.8	0.28	182.79	5.2	mild	4.97	mild	yes
31-0	3143.40	3.5	45.63	462.35	15.6	moderate	24.65	severe	no
31-1	6387.95	3.81	69.46	642.62	29.4	severe	28.89	severe	yes
31-2	3339.48	3.52	38.72	478.82	13.3	moderate	7.15	moderate	yes
45-0	3918.99	3.59	40.71	359.38	30	severe	27.24	severe	yes
45-1	1922.61	3.28	21.72	463.62	3.6	mild	6.17	mild	yes
45-2	1518.71	3.18	15.58	233.79	3.3	mild	6.41	mild	yes
59-0	584.40	2.77	6.67	176.61	15.4	moderate	13.50	moderate	yes
59-1	706.63	2.85	4.01	202.6	5.95	mild	5.13	mild	yes
59-2	635.44	2.8	1.62	188.93	4.6	mild	4.96	mild	yes
61-0	388.95	2.59	0.65	360.72	7.1	moderate	8.38	moderate	yes
61-1	139.65	2.15	0.02	356.7	1.3	mild	1.85	mild	yes
61-2	40.89	1.61	0.02	151.4	3.2	mild	0.25	mild	yes
68-1	522.38	2.72	0.02	348.63	3.8	mild	4.18	mild	yes
83-0	2844.69	3.45	108.86	182.79	25.5	severe	26.93	severe	yes
83-1	868.67	2.94	0.02	131.91	0.6	mild	5.68	mild	yes
83-2	843.24	2.93	0.02	1.61	0.1	mild	6.01	mild	yes

Serum TARC, IL-22 and sIL-2R levels in serum of AD patients are used to predict EASI scores before treatment (t0) and after treatment (t1) by the signature $EASI = (-36.1180 + 18.4941 \cdot \log TARC + 0.008942 \cdot IL-22 - 0.00946 \cdot sIL-2R) \cdot (1 - \text{treatment}) - (5.8183 + 4.0392 \cdot \log TARC + 0.002739 \cdot IL-22 - 0.00284 \cdot sIL2R) \cdot \text{treatment}$, in which treatment can be either No=0, or Yes=1. Both EASI and predicted EASI scores are classified as mild (1.0-7.0), moderate (7.1-21.0) or severe (>21.1).