Supplementary Figure Legends

Supplementary Figure E1. **A)** Photographs from a representative patient at wks 0, 2, and 12 after cyclosporine 5mg/kg/day treatment. **B)** Significant reductions in SCORAD of 50.89% and 73.44% were observed at wks 2 and 12 after CsA. **C)** Total IgE and **(D)** eosinophil serum levels at wks 2 and 12 of CsA. *pre vs post p-values are indicated. Wk/week; Mean±SEM*

Supplementary Figure E2. Reductions in cellular infiltrates by immunohistochemistry, in lesional/LS and non-lesional/NL atopic dermatitis at wks 2 and 12 of CsA. Representative staining is shown, with significant reductions in CD3+ T-cells **(A,E)**, myeloid/CD11c+ **(B,F)**, CD206+ **(C,G)**, and mature/CD83+ dendritic cells **(D,H)** at wks2 and 12. *Wk/week; Mean±SD, *p<0.05/**p<0.01/***p<0.001*

Supplementary Figure E3. Changes in a transcriptome subset of immune genes **(A)**. AD transcriptome improves by 84.25% and 105.95% at wks 2 and 12 respectively **(B)**. *Red/upregulated; Blue/downregulated; Wk/week; AD/atopic dermatitis. Heatmap is arranged by patient SCORAD (white to black gradient) pink = patients with unknown SCORAD.*

Supplementary Figure E4. Representative S100A7 staining at wks 0 and 12 LS and NL skin **(A)**. Representative 40X magnification H&E **(B)**, arrow points to

absence of granular layer at wk 0 and restoration of granular layer at wk 12. Representative IHC of **C)** filaggrin and **D)** loricrin after treatment in LS and NL AD (n=5/antibody). *Wk/week; LS/lesional; NL/non lesional; AD/atopic dermatitis; FLG/filaggrin; LOR/loricrin.*

Supplementary Figure E5. Quantitative RT-PCR of several Th2-related cytokines. **A-D)** mRNA differences from baseline expression levels (fold-changes/FCHs) in lesional/LS and non-lesional/NL skin at wks2 and 12 of treatment. *Wk/week; pre vs post p-values are indicated; Mean±SEM*

Supplementary Figure E6. Small increases in mRNA expression of differentiation genes filaggrin/FLG **(A)**, loricrin/LOR **(B)** and periplakin/PPL **(C)**, particularly at wk2. *FCH/fold changes; Wk/week; pre vs post p-values are indicated; Mean±SEM*

Supplementary Figure E7. Comparison of selected cellular **(A)** and genomic **(B)** biomarkers between non-responders and responders at weeks 2 (W2) and 12 (W12) of treatment. Color corresponds to treatment effect on LS skin (W12 vs W0) in responders. Y-axis shows differences between responders and non-responders. For example, IL-13 decreased by 5.1 $\log_2$FCH at W12 in the responder group, whereas it only slightly increased by 0.5 $\log_2$FCH in the non-responder group, corresponding to a difference of 5.6 between the two groups. *W/week; LS/lesional; FCH/fold change*

Supplementary Figure E8. Scatterplots corresponding to the top Spearman correlations in Table E4A-B.

Supplementary Table E1. Demographic data of the atopic dermatitis patients enrolled in this study, including gender, patient age, race, SCORAD, total serum IgE, and % eosinophils at baseline, wks 2 and 12, and filaggrin mutation status. *Wk/Week; Scoring of AD/SCORAD.*

Supplementary Table E2. Effects of CsA on the AD transcriptome. The FCHs, $\log_2$FCHs, p-values, and status (1=up-regulated, -1=down-regulated, 0=not differentially expressed) are indicated for each comparison, including post versus pre-treatment values at wks 2 and 12 for LS and NL skin, and LS versus NL skin at wks 2 and 12. *DEGs/differentially-expressed genes; LS/lesional; NL/non-lesional; FCH/fold change.*

Supplementary Table E3. Average mRNA expression values and confidence interval values corresponding with Figure 3.

Supplementary Table E4. LS skin biomarkers significantly correlated with improvement in the SCORAD index following CsA. Spearman rank correlations were determined for all evaluated biomarkers quantified by immunohistochemistry (denoted by “I”) and real-time-PCR (RT-PCR) (denoted by

"R") with reduction in SCORAD **(A)** and epidermal thickness **(B)** following treatment. FDR <0.03 (A) and <0.02 (B).

Supplementary Table E5. Antibodies (with specific vendor, clone, isotype, and dilution value) used in immunohistochemistry.

Supplementary Table E6. Comparison of mRNA expression differences (FCHs) in pre (Wk0) and post (Wk12 or D56) LS skin biopsies from psoriasis and atopic dermatitis patients treated with CsA. Psoriasis data is from (Haider et al., J Immunol 2008 180(3):1913-20) *AD/atopic dermatitis; PsO/psoriasis; LS/lesional; Wk/week; D/day; FCH/fold change; ND/not done.*

Table E1: Characteristics of study patients

Patient #	Gender	Age	Race[a]	SCORAD[b] Baseline	IgE[c] Baseline	Eos %[d] Baseline	SCORAD Week 2	IgE Week 2	Eos % Week 2	SCORAD Week 12	IgE Week 12	Eos % Week 12	FLG*
1	M	32	A	84.5	70530	17.3	64.5	54729	6.7	27	69068	10	
2	M	18	A	73.5	2615	12.1	44.5	1825	9.6	37	2500	17	
3	M	32	C	74.5	3812	8.9	20	4129	5.3	16	3560	12.5	
4	M	59	C	97	5376	16.6	46.5	3985	8.2	39.5	3443	7.5	
5	M	32	A	54	745	12.3	43.5	583	8	25.5	562	6.1	
6	M	63	C	98	6033	11.6	58	5538	17.2	16.1	8397	5.7	Negative
7	M	34	C	76	100	4.2	76	100	4.2	59	151	3.7	Negative
8	M	33	C	66	1281	9.6	5.9	1427	5.25	0	948	4.1	Negative
9	M	45	C	56	1281.5	2.6	15	360	1.2	8	1600.9	2.5	
10	F	49	C	56	1304	8	24	1605	5.7	8	763	5.9	
11	M	48	C	51	41	3.6	18	28	2.6	7	20	3.1	Negative
12	F	59	C	45	14.1	1.4	NA	NA	NA	15	11.7	1.6	Negative
13	F	50	C	44	1269	6.3	21	820	6	7	1100	5.2	Negative
14	F	67	C	53	6	0.6	14	5	1.1	6	5	2.2	
15	F	40	C	72	92.2	2.9	40	57.5	1.3	15	43	1.6	
16	F	59	C	56	3.6	3.5	16	4.2	1.7	6	4	1.9	
17	M	69	C	61	72.9	2.36	NA	NA	NA	20	65	2.7	
18	F	36	C	65	492	11.8	26	365	7.6	18	258	6.4	
19	M	42	C	53	1821	9.2	34	1230	7.1	10	211	4.3	

* If not indicated, Filaggrin genotyping was not performed (see supplementary methods)
a: A = African American C = Caucasian
b: SCORing of Atopic Dermatitis (see Methods)

c: Reference range, 0-114kU/L
d: Reference range, 0-7% serum eosinophil count

Probe	Symbol	Description
229476_s_at	THRSP	thyroid hormone responsive
229477_at	THRSP	thyroid hormone responsive
205030_at	FABP7	fatty acid binding protein 7, brain
239929_at	PM20D1	peptidase M20 domain containing 1
214240_at	GAL	galanin/GMAP prepropeptide
205029_s_at	FABP7	fatty acid binding protein 7, brain
234980_at	TMEM56	transmembrane protein 56
1569909_at	KRT79	keratin 79
229151_at	SLC14A1	olute carrier family 14 (urea transporter), member 1 (Kidd blood group
220801_s_at	HAO2	hydroxyacid oxidase 2 (long chain)
234513_at	ELOVL3	ELOVL fatty acid elongase 3
202218_s_at	FADS2	fatty acid desaturase 2
204607_at	HMGCS2	3-hydroxy-3-methylglutaryl-CoA synthase 2 (mitochondrial)
239108_at	FAR2	fatty acyl CoA reductase 2
203400_s_at	TF	transferrin
227762_at		
207670_at	KRT85	keratin 85
206243_at	TIMP4	TIMP metallopeptidase inhibitor 4
243168_at		
231262_at		
205883_at	ZBTB16	zinc finger and BTB domain containing 16
230964_at	FREM2	FRAS1 related extracellular matrix protein 2
1555318_at	HIF3A	hypoxia inducible factor 3, alpha subunit
233932_at		
222124_at	HIF3A	hypoxia inducible factor 3, alpha subunit
208962_s_at		
204416_x_at	APOC1	apolipoprotein C-I
228409_at	PLIN4	perilipin 4

Table E3	RT-PCR average expression values and confidence intervals											
Gene	**Wk2 vs**	**LCI**	**UCI**	**Wk12 vs**	**LCI**	**UCI**	**Wk2 vs**	**LCI**	**UCI**	**Wk12 vs**	**LCI**	**UCI**
	Wk0 (LS)			**Wk0 (LS)**			**Wk0 (NL)**			**Wk0 (NL)**		
MMP12	-2.27	-3.73	-0.82	-3.54	-5	-2.09	-0.47	-1.97	1.03	-1.49	-2.99	0.01
S100A12	-2.75	-4.28	-1.22	-4.47	-6	-2.94	-0.73	-2.3	0.84	-1.63	-3.2	-0.05
IL-13	-2.72	-4.47	-0.97	-4.21	-5.97	-2.47	-3.18	-4.98	-1.4	-3.47	-5.27	-1.67
IL-19	-2.87	-4.24	-1.5	-3.73	-5.1	-2.36	-0.44	-1.85	0.96	-1.9	-3.3	-0.49
CCL13	-1.33	-2.31	-0.36	-0.98	-1.96	-0.01	-1.63	-2.63	-0.6	-1.76	-2.76	-0.76
CCL17	-2.36	-3.28	-1.43	-2.12	-3.06	-1.2	-0.62	-1.58	0.33	-0.66	-1.61	0.29
CCL18	-1.71	-2.61	-0.81	-2.6	-3.5	-1.71	-1.41	-2.33	-0.5	-2.16	-3.09	-1.24
IL-9	-3.21	-4.4	-2.03	-3.17	-4.36	-1.98	-0.99	-2.22	0.22	-1.07	-2.3	0.14
IL-22	-2.23	-3.48	-0.98	-3.42	-4.67	-2.17	-1.18	-2.47	0.1	-1.68	-2.96	-0.4
S100A7	-1.94	-2.81	-1.07	-2.97	-3.84	-2.1	-0.89	-1.79	-0	-1.19	-2.08	-0.3
S100A8	-1.86	-3	-0.72	-2.76	-3.9	-1.62	-0.45	-1.62	0.72	-1.13	-2.31	0.04
S100A9	-2.44	-3.32	-1.55	-3.25	-4.14	-2.36	-0.5	-1.42	0.41	-0.91	-1.83	-0
IFNy	-2.09	-7.14	2.95	-0.5	-5.55	4.539	-0.51	-4.54	5.55	-1.02	-6.07	4.02
CXCL9	-2.33	-3.19	-1.48	-2.52	-3.37	-1.67	-1.21	-2.08	-0.3	-1.53	-2.4	-0.65
CXCL10	-2.15	-3.29	-1.01	-2.32	-3.46	-1.18	-0.81	-1.98	0.36	-1.53	-2.69	-0.36
MX1	-0.93	-1.38	-0.49	-1.11	-1.56	-0.67	-0.16	-0.61	0.3	-0.06	-0.52	0.4
STAT1	-0.64	-0.99	-0.3	-0.94	-1.28	-0.59	-0.4	-0.75	-0	-0.29	-0.64	0.07
IL-1B	-1.16	-1.91	-0.41	-0.62	-1.37	0.132	0.26	-0.51	1.03	-0.11	-0.88	0.67
IL-8	-2.58	-3.93	-1.22	-3.08	-4.43	-1.73	-1.14	-2.53	0.25	-1.44	-2.83	-0.05
IL-17A	-0.61	-1.4	0.182	-0.95	-1.74	-0.16	-0.54	-1.35	0.28	-0.18	-1	0.63
IL-12B	-1.22	-2.63	0.186	-2.1	-3.51	-0.7	-0.29	-1.74	1.16	-0.42	-1.87	1.02
CXCL1	1.57	-2.19	-0.95	-2.16	-2.78	-1.53	-0.22	-0.86	0.42	-0.18	-0.82	0.46
CCL20	-1.47	-2.44	-0.51	-1.94	-2.9	-0.97	-0.36	-1.35	0.63	-0.87	-1.86	0.12
PI3	-2.41	-3.83	-1	-3.08	-4.49	-1.66	-1.18	-2.63	0.28	-1.74	-3.19	-0.28
LCI/ lower confidence interval; UCI/upper confidence interval; LS/ lesional; NL/ non-lesional; Wk/week												

Table E4. Correlation of reduction of inflammatory markers and epidermal biomarkers with disease improvement following CsA

A. Lesional skin biomarkers significantly correlated with improvement in the SCORAD index following CsA

Disease Biomarkers in LS Skin	Spearman Correlation	P-value
S100A7 (R)	0.58	<0.001
IL-13 (R)	0.51	<0.001
IL-22 (R)	0.51	<0.01
MMP12 (R)	0.50	<0.01
CCL26 (R)	0.49	<0.01
S100A9 (R)	0.48	<0.01
CCL18 (R)	0.47	<0.01
CCL17 (R)	0.45	<0.01
CD206 (I)	0.43	<0.01
CD3 (I)	0.42	<0.01
Epidermal Thickness (I)	0.42	<0.01
S100A12 (R)	0.42	<0.01
CXCL10 (R)	0.42	<0.01
CD83 (I)	0.41	<0.05
CCL22 (R)	0.41	<0.05

B. Lesional skin biomarkers significantly correlated with reduction of epidermal thickness following CsA

Disease Biomarkers in LS Skin	Spearman Correlation	P-value
K16 (R)	0.65	<0.001
IL-13 (R)	0.57	<0.001
S100A7 (R)	0.56	<0.001
S100A9 (R)	0.55	<0.001
PI3 (R)	0.53	<0.001
S100A12 (R)	0.53	<0.001
CD83 (I)	0.52	<0.001
S100A8 (R)	0.48	<0.01
IL-19 (R)	0.47	<0.01
MMP12 (R)	0.43	<0.01
SCORAD Improvement	0.42	<0.01
SCORAD	0.42	<0.01

Table E5. Antibodies used for immunohistochemical analysis

Antibody	Vendor	Clone	Isotype	Dilution
Keratin 16 (K16)	Serotec	LL025	IgG1	1:100
Ki67	Santa Cruz	MIB-1	IgG1	1:100
CD3	BD Biosciences	SK7	IgG1	1:100
CD11c	BD Biosciences	B-ly6	IgG1	1:100
CD206	Genetex	15-2	IgG1	1:100
CD83	BD Biosciences	HB15e	IgG2	1:20
FLG	Acris	FLG01	IgG1	1:500
LOR	Abcam	Ab24722	IgG2	1:500
S100A7	Abcam	47C1068	IgG1	1:250

Table E6

	AD (LS)		PsO (LS)	
	Wk2 vs Wk0	**Wk12 vs Wk0**	**Wk2 vs Wk0**	**D56 vs Wk0**
	(FCH)	**(FCH)**	**(FCH)**	**(FCH)**
K16	-4	-6.1	-3.75	-7.5
General Inflamation				
S100A12	-6.7	-22.2	-4	-20
MMP12	-4.8	-11.7	-5	-10
Innate Immunity				
IL-8	-6	-8.5	-15	-30
IL-1β	-2.2	-1.5	-7.5	-15
Th2-related				
IL-13	-6.6	-18.6	ND	ND
IL-19	-7.3	-13.3	-2	-6
CCL18	-3.3	-6.1	ND	ND
CCL17	-5.1	-4.4	ND	ND
CCL13	-2.5	-2	ND	ND
Th9				
IL-9	-9.3	-9	ND	ND
Th22				
IL-22	-4.7	-10.7	-5	-5
Th1/Interferon				
MIG/CXCL9	-5	-5.7	-5	-6.67
IP10/CXCL10	-4.4	-5	-2.53	-9.6
IFNγ	-1.8	-2.4	-1.5	-2
MX1	-1.9	-2.2	-1.56	-7
STAT1	-1.6	-1.9	-1.83	-2
IL-17				
IL-12β/IL-23p40	-2.3	-4.3	-7.5	-15
CCL20	-2.8	-3.8	-2	-8
IL-12A/IL-23p19	1.1	-1.1	-6	-7.5
IL-17	-1.5	-1.9	-2	-6

Figure E1

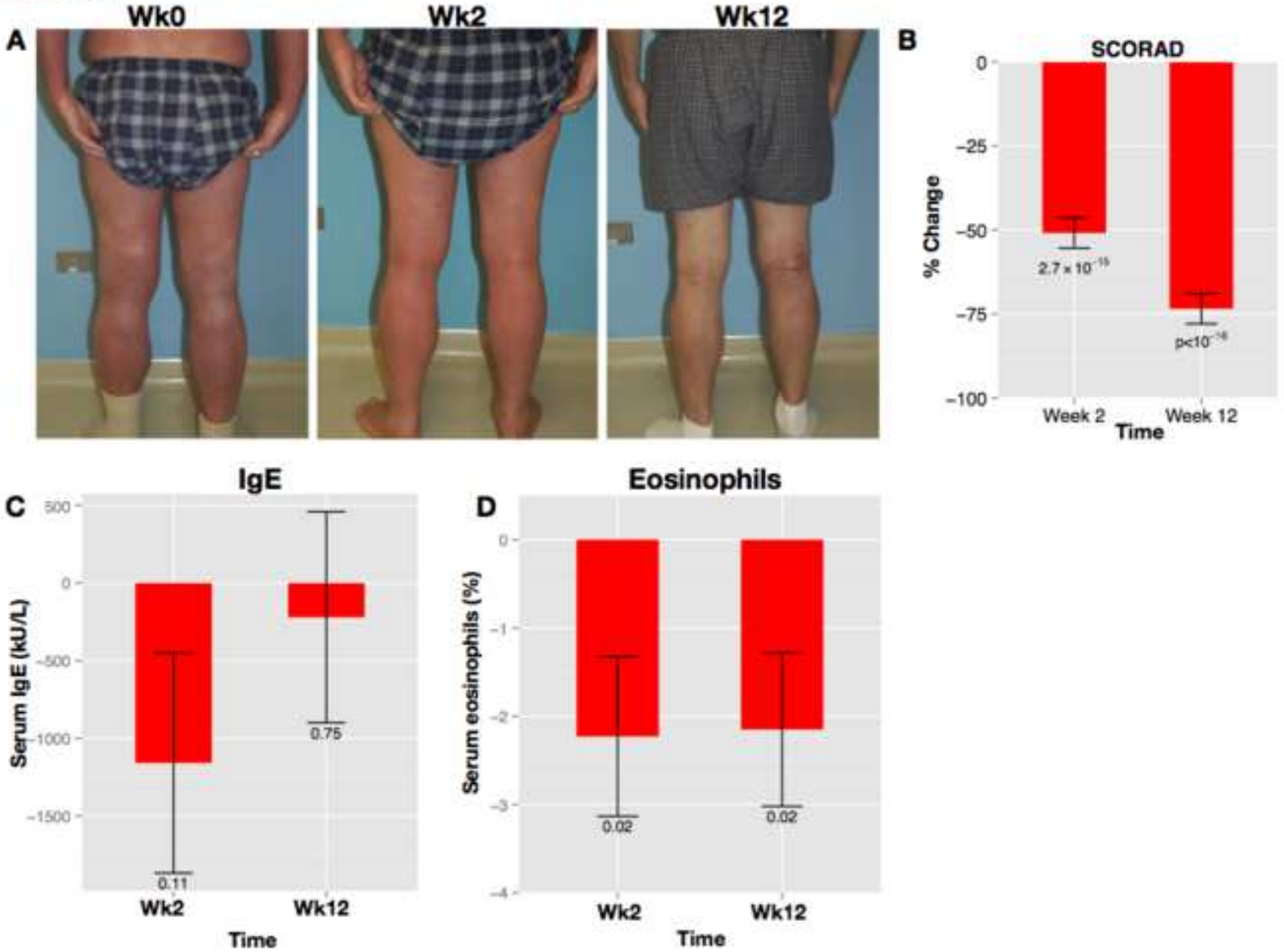
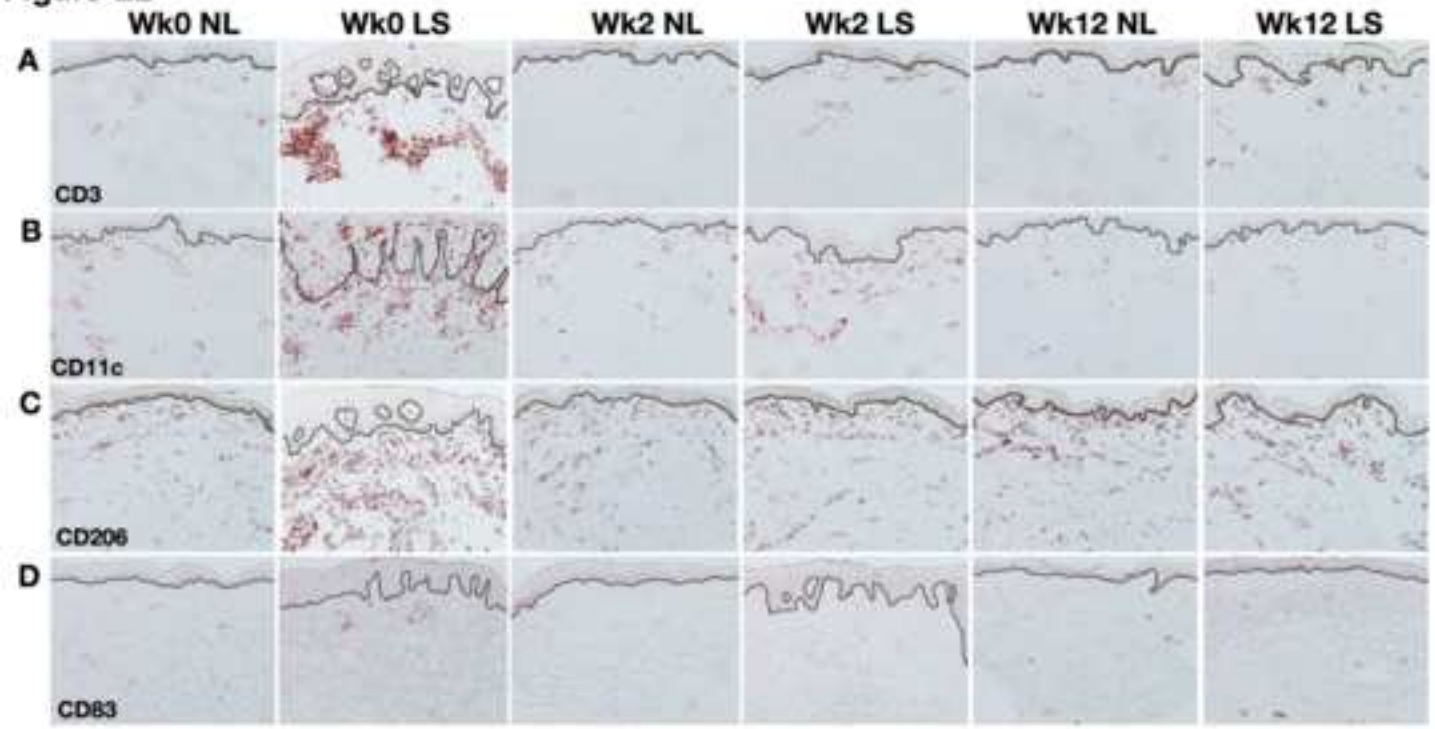
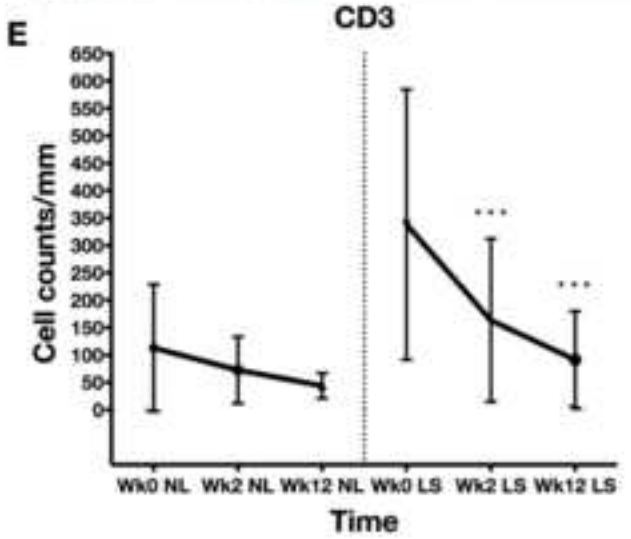
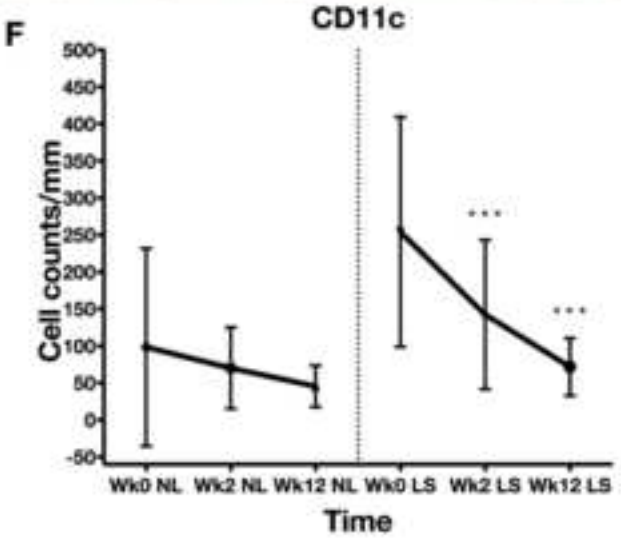
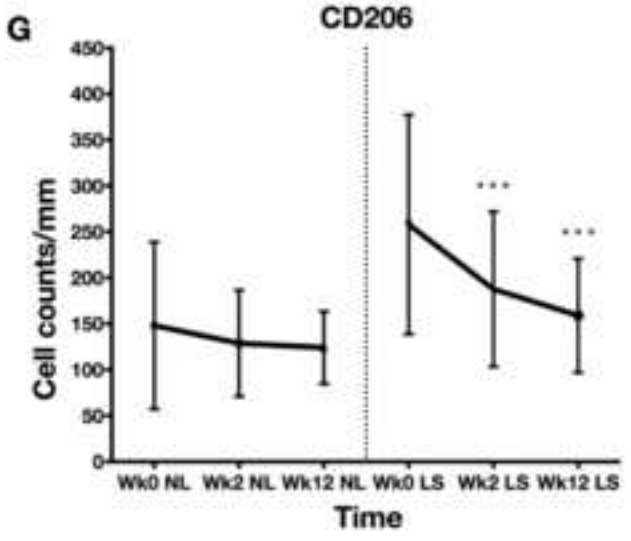


Figure E2









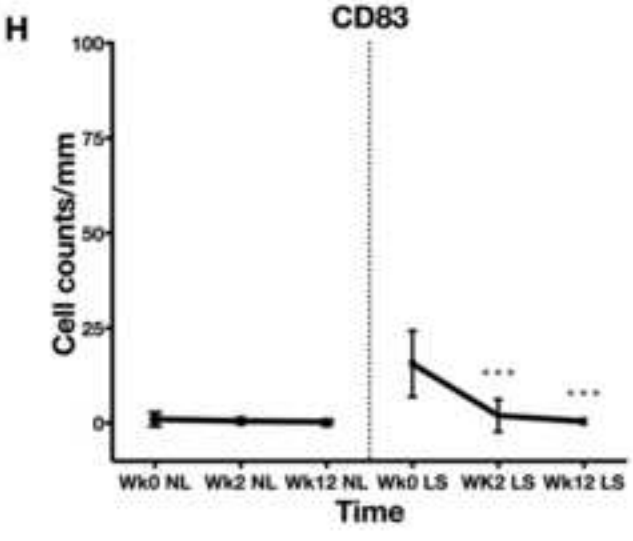


Figure E3

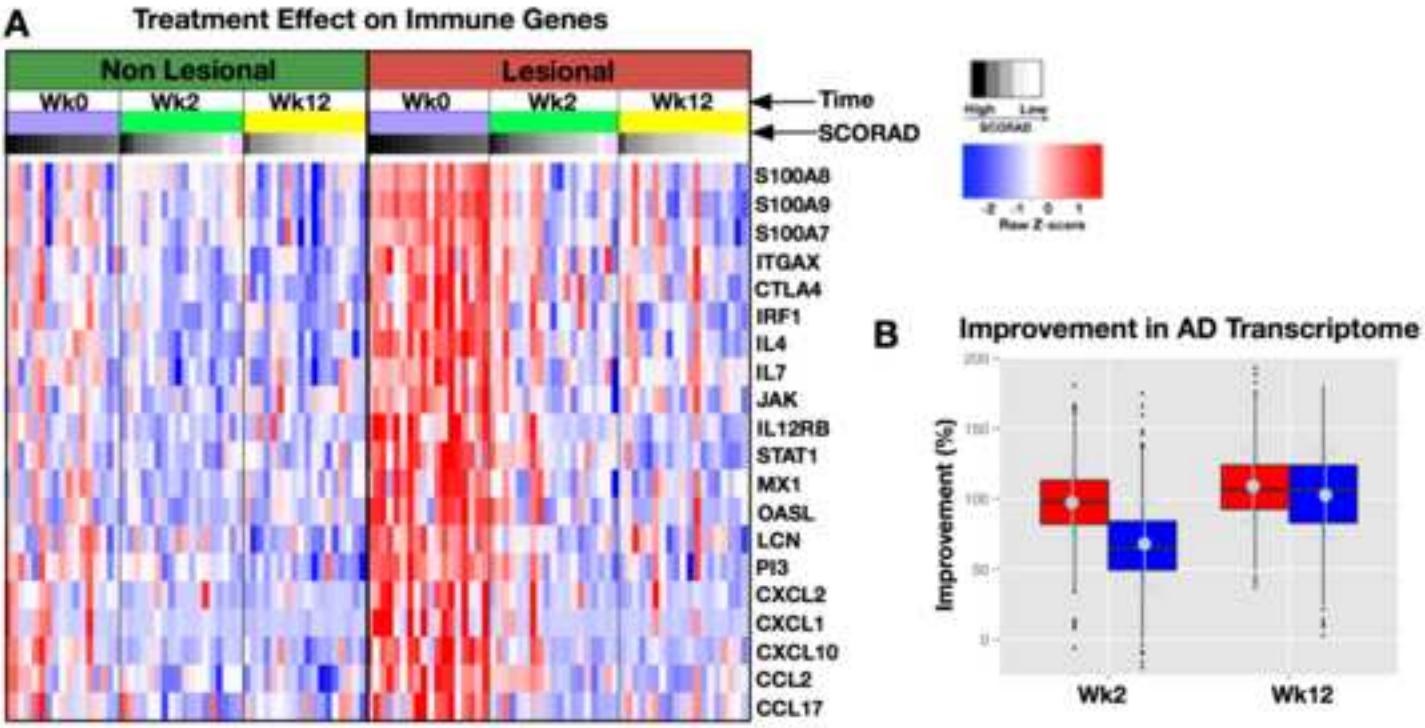
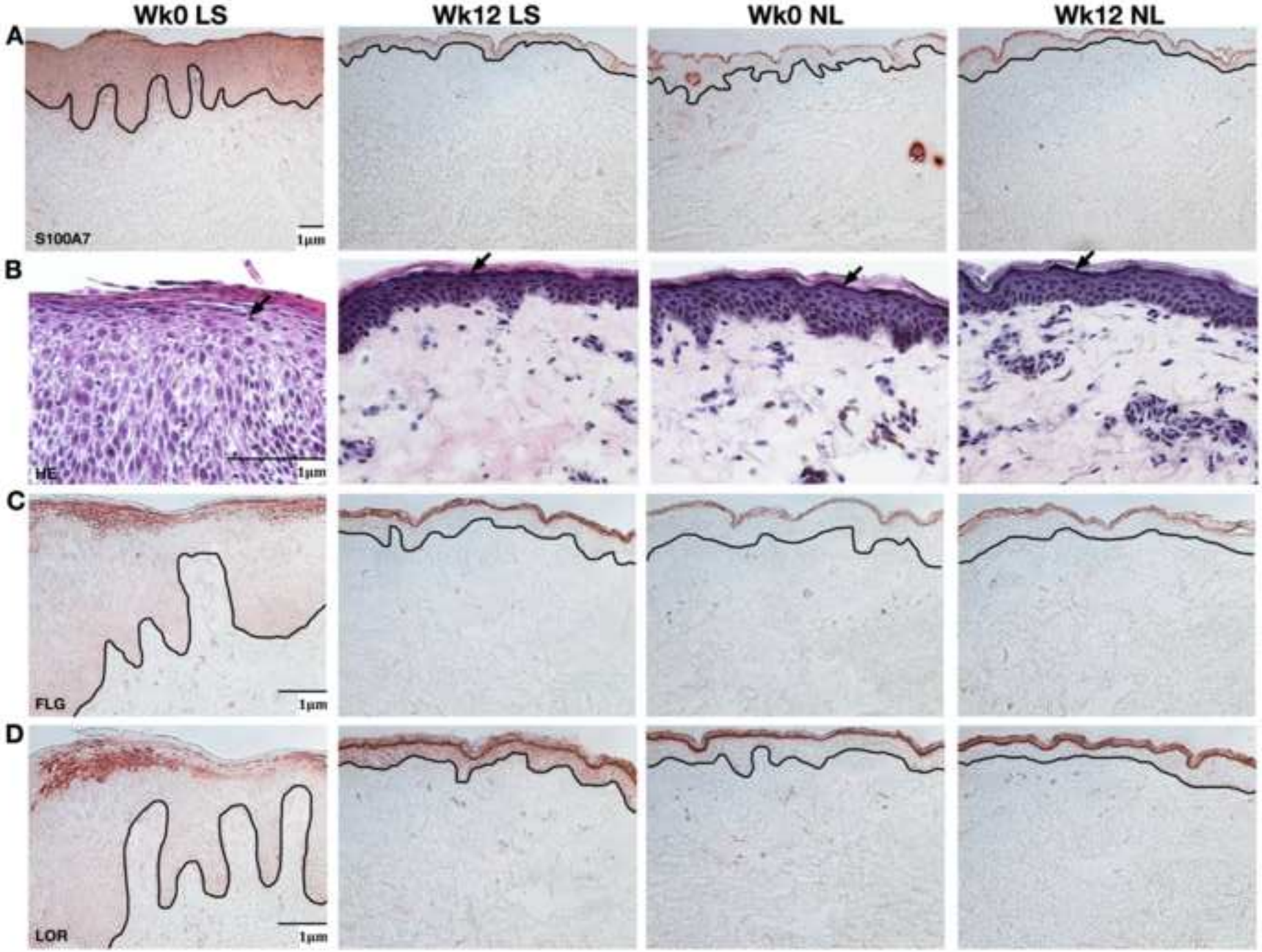


Figure E4



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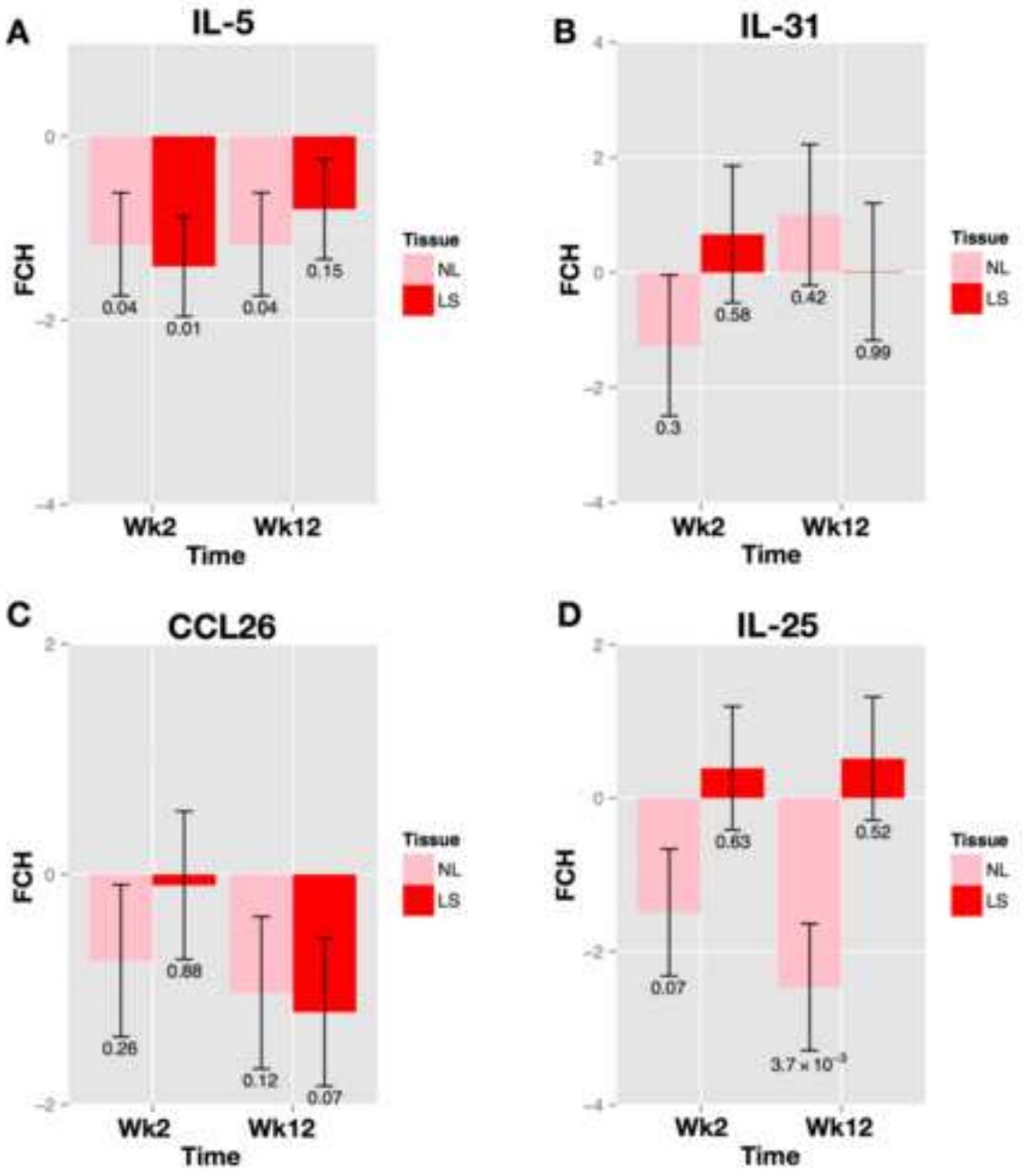

Figure E6

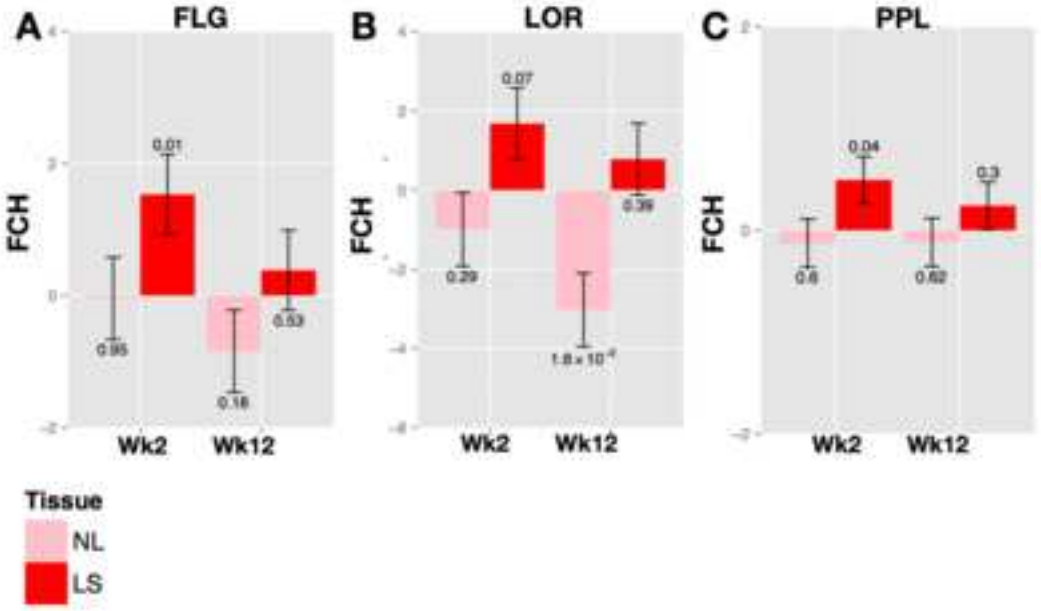

Figure E7

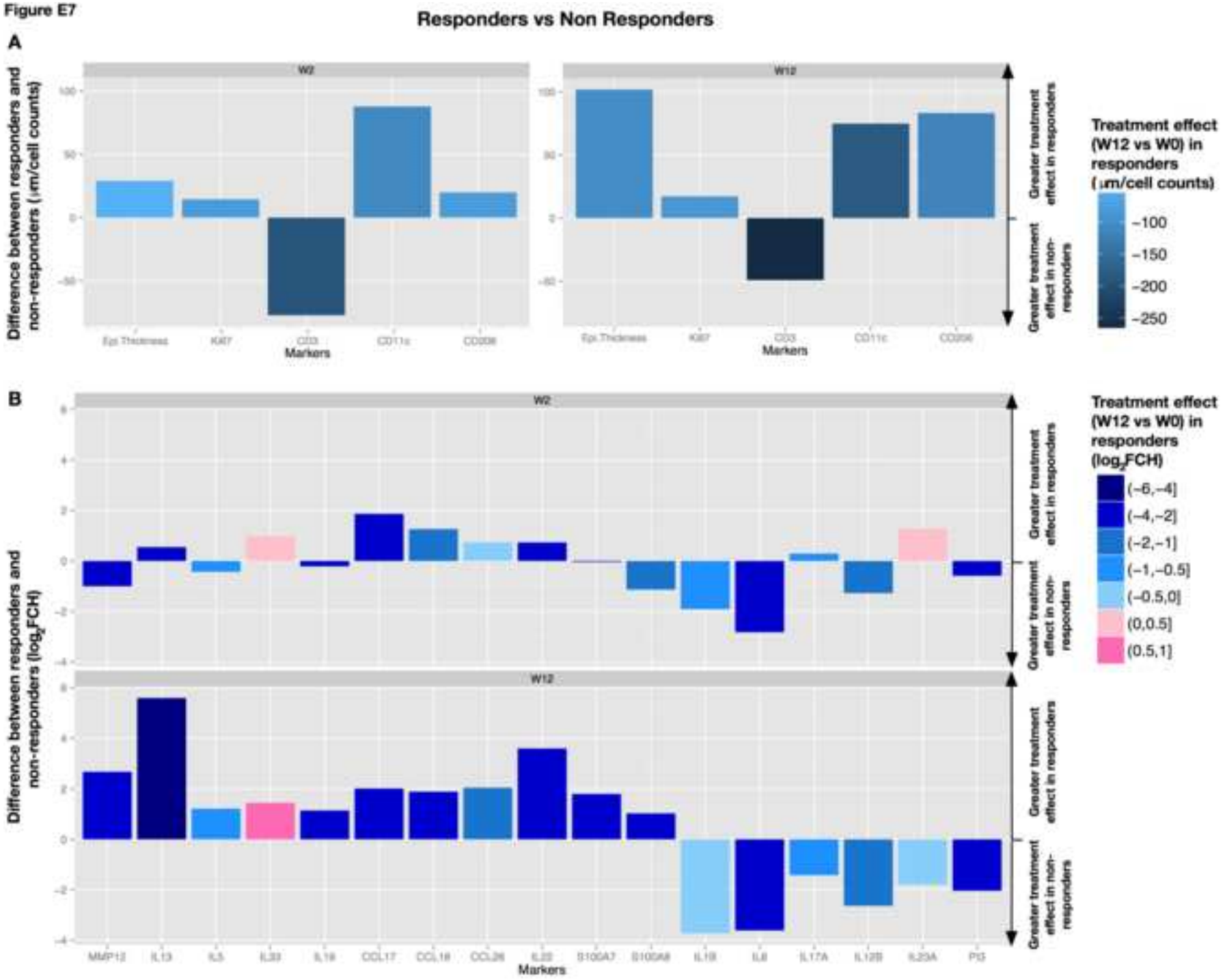

Figure E8