

Topical Nitric Oxide Releasing Therapy with SB414 2% Cream Downregulated Major Gene Expressions in Patients with Atopic Dermatitis

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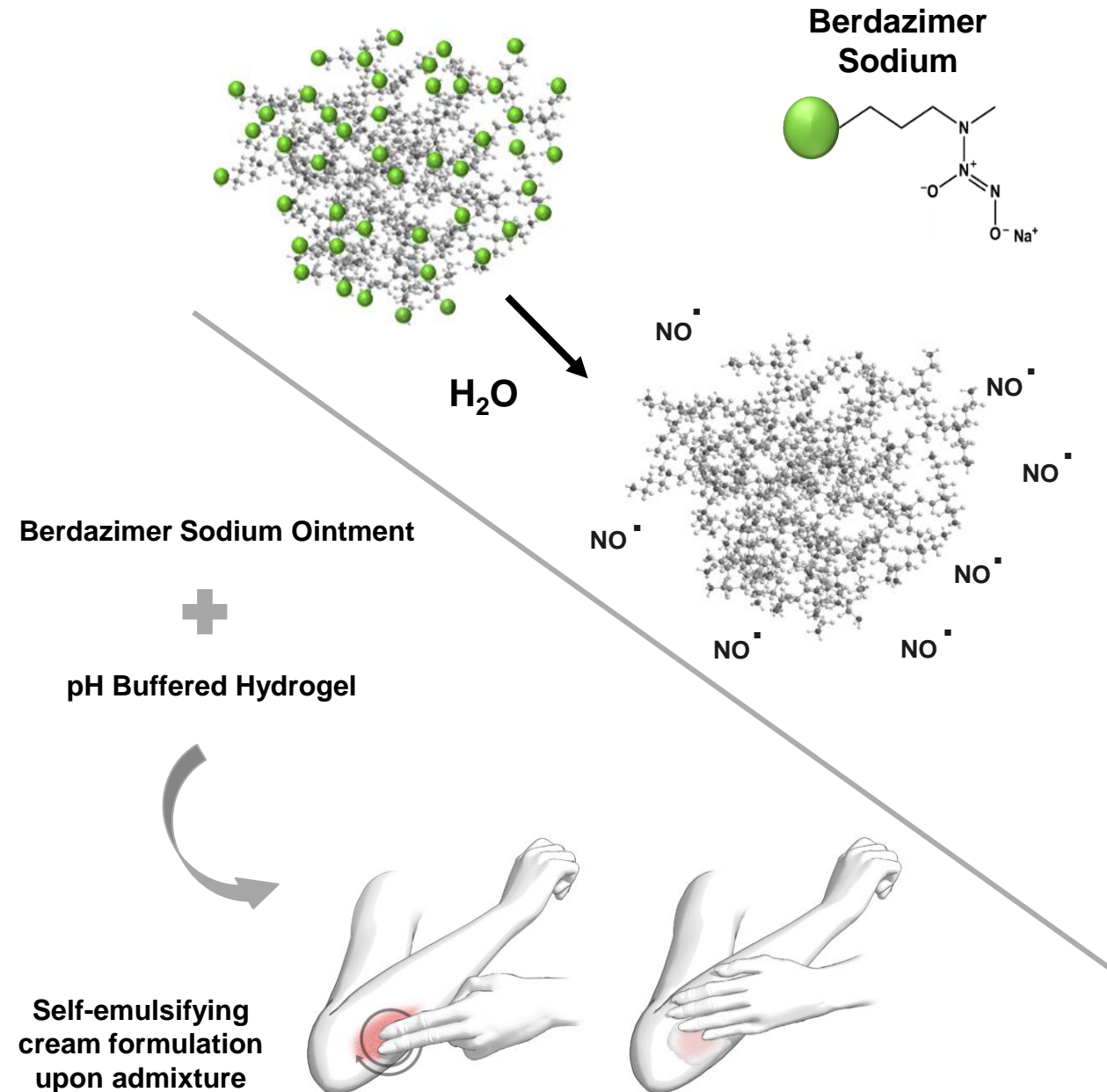
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Nitric Oxide, Berdazimer Sodium and SB414

- Nitric oxide (NO) is an endogenous small molecule
 - Short-lived immune modulator
 - Direct broad-spectrum antimicrobial agent
- Berdazimer sodium is a macromolecule comprised of a polysiloxane backbone with covalently bound N-diazeniumdiolate NO donors
- Co-administration with a proton donor
 - Promotes NO release from the macromolecule
- SB414 is an investigational product that consists of two components
 - Ointment containing berdazimer sodium
 - Hydrogel



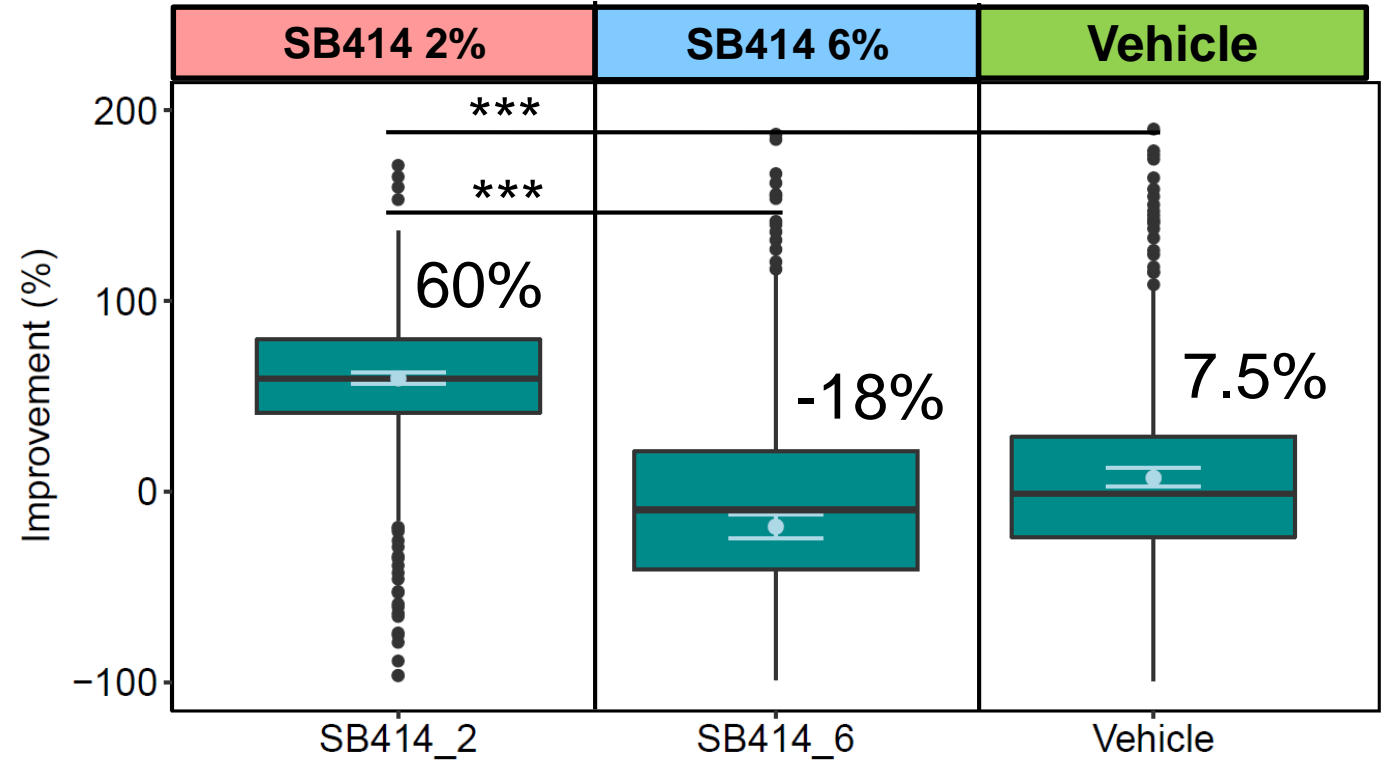
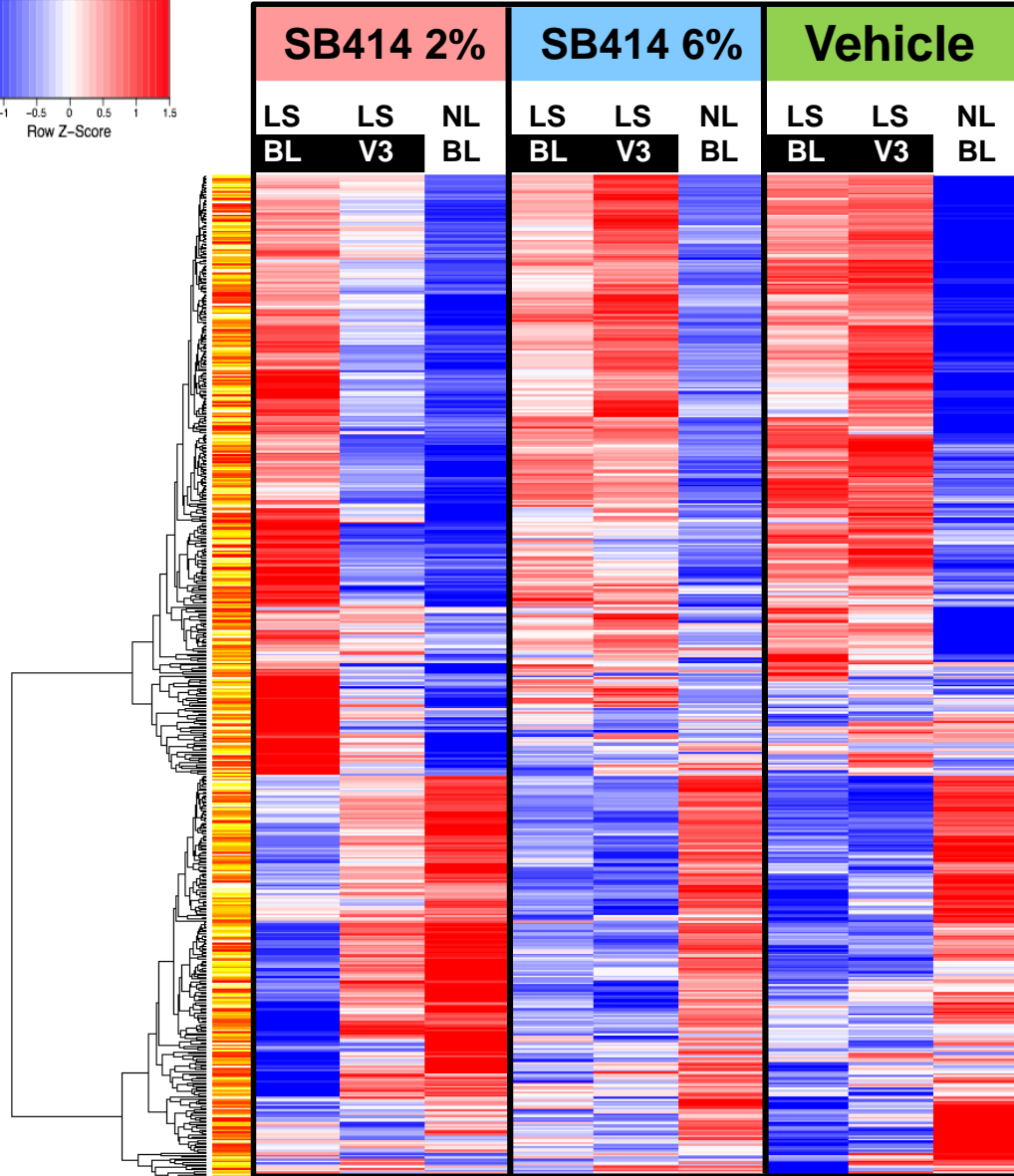
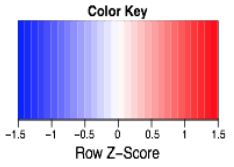
Phase 1b Trial Design for Atopic Dermatitis (AD-101)

Description	<ul style="list-style-type: none">▪ Multi-center, randomized, double-blind, vehicle-controlled trial to evaluate the PK/PD, safety, and tolerability of SB414 for the treatment of atopic dermatitis
Trial Design	<ul style="list-style-type: none">▪ 48 subjects▪ 2:1 (active:vehicle) randomization▪ Active arms: SB414 2%, SB414 6%▪ 14 day wash out period prior to randomization▪ Subjects will apply the study drug (SB414 or Vehicle) to affected areas twice daily for 2 weeks (14 days)
Key Inclusion Criteria	<ul style="list-style-type: none">▪ Male or female, 18 years of age and older▪ EASI score >1 and ≤21, involving ≥5% body surface area (BSA)
Study Objectives	<ul style="list-style-type: none">▪ Assess IL-4, IL-5, IL-13, and other key inflammatory cytokines▪ Safety and cutaneous tolerability (investigator and subject assessment)▪ Systemic exposure via PK assessments of berdazimer sodium on Day 1 and Day 14▪ Efficacy as measured by EASI (Eczema Area and Severity Index) score and Itch NRS (a 10-point numerical rating scale reported by the patient)

AD-101 Study Clinical Results

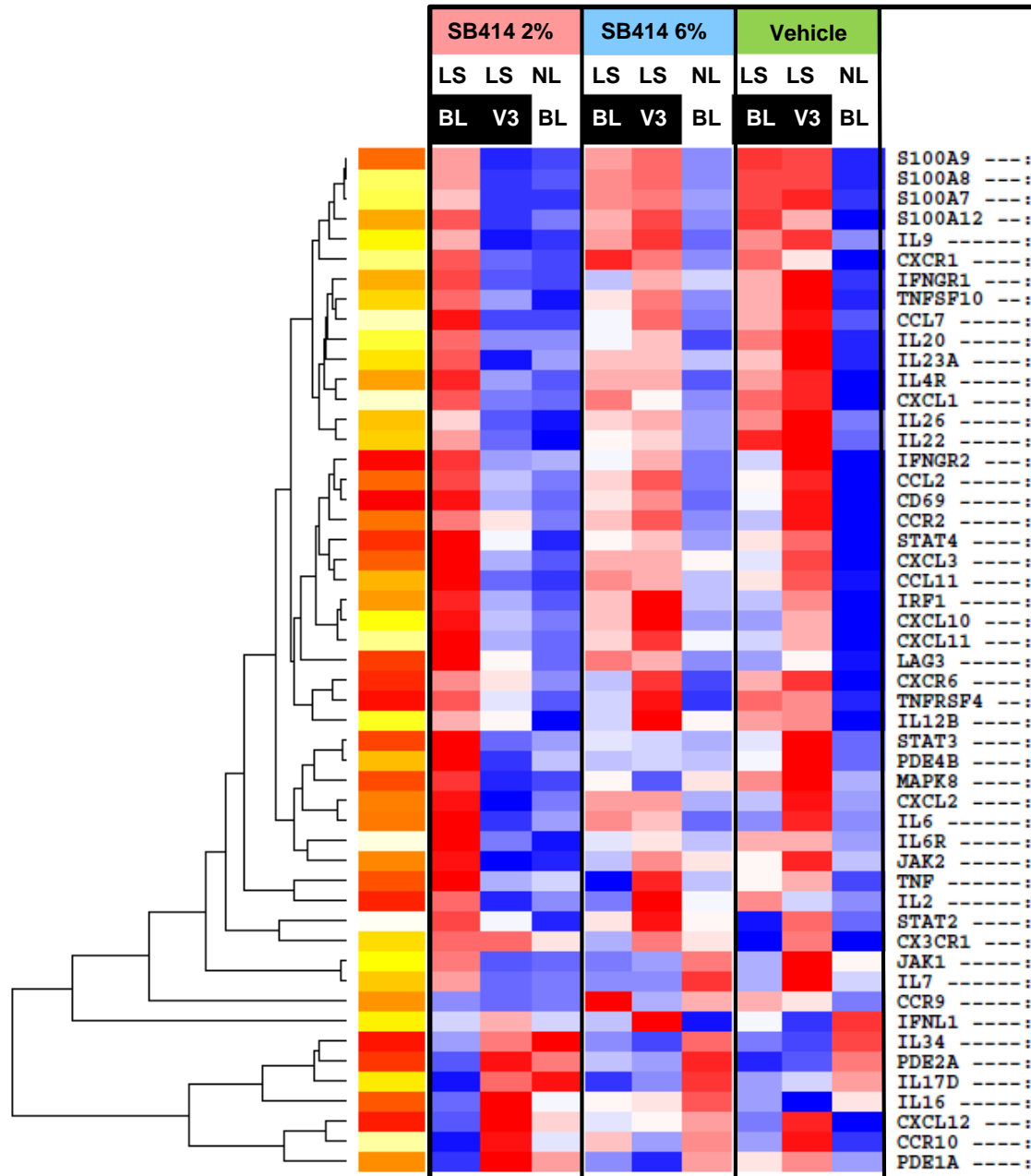
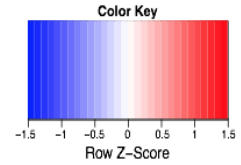
	Vehicle	SB414 2%	SB414 6%
EASI Score at Baseline			
N	14	17	17
Mean (SD)	8.2 (5.2)	4.7 (2.0)	7.2 (3.3)
Median	8.1	4.4	6.2
Percent Change from Baseline in EASI Score			
N	13	17	17
Mean (SD)	-21.41 (29.01)	-23.22 (29.14)	-21.63 (51.80)
Median	-15.79	-28.57	-25.81
Baseline Itch Score			
N	14	17	17
Mean (SD)	6.3 (1.7)	6.9 (2.2)	6.4 (2.1)
Median	7.0	8.0	7.0
Minimum, Maximum	3, 9	0, 9	3, 10
Itch NRS Change from Baseline			
N	13	17	17
Mean (SD)	-2.31 (2.78)	-3.47 (2.43)	-3.12 (2.78)
Median	-2.00	-4.00	-3.00
Itch Reduction Responders			
Itch Reduction ≥ 3	6 (43%)	12 (71%)	10 (59%)
Itch Reduction ≥ 4	4 (29%)	10 (59%)	7 (41%)

LS vs NL Transcriptome Improvement from Baseline (FCH>2, FDR<0.05)

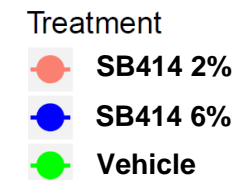
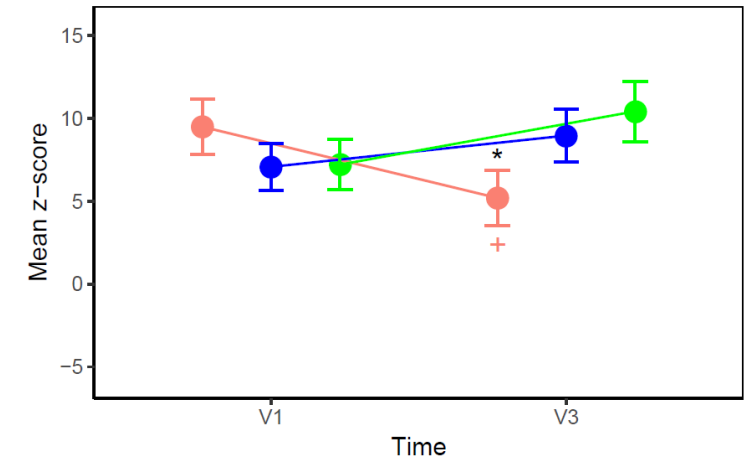


FCH: Fold Change
FDR: False Discovery Rate (adjusted p-values)

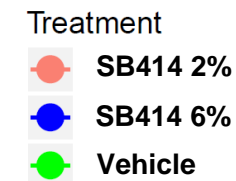
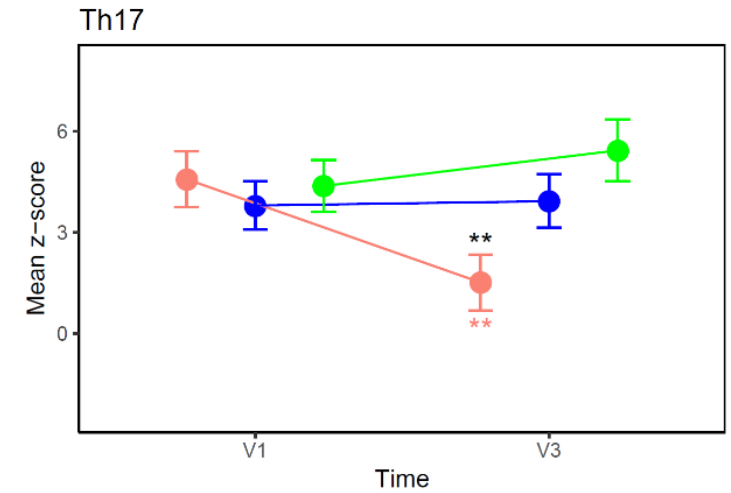
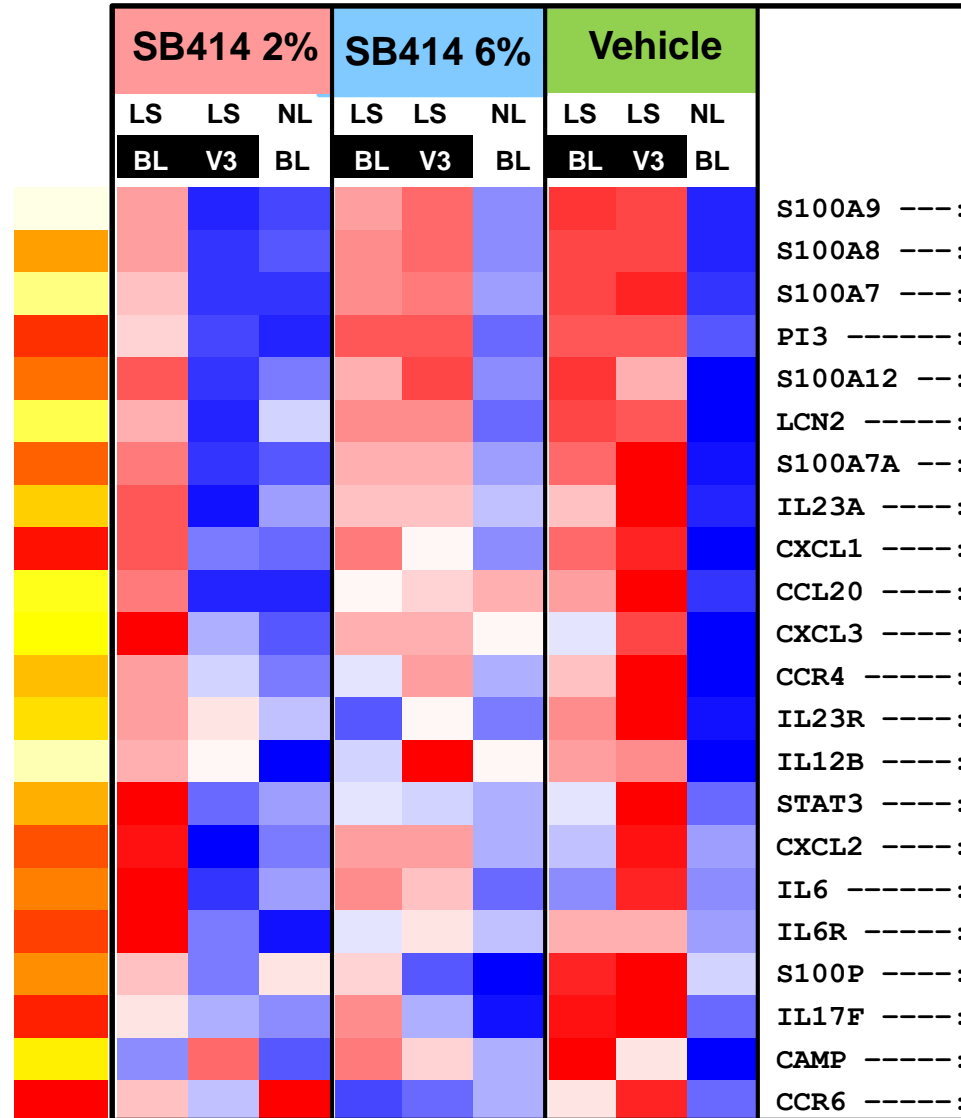
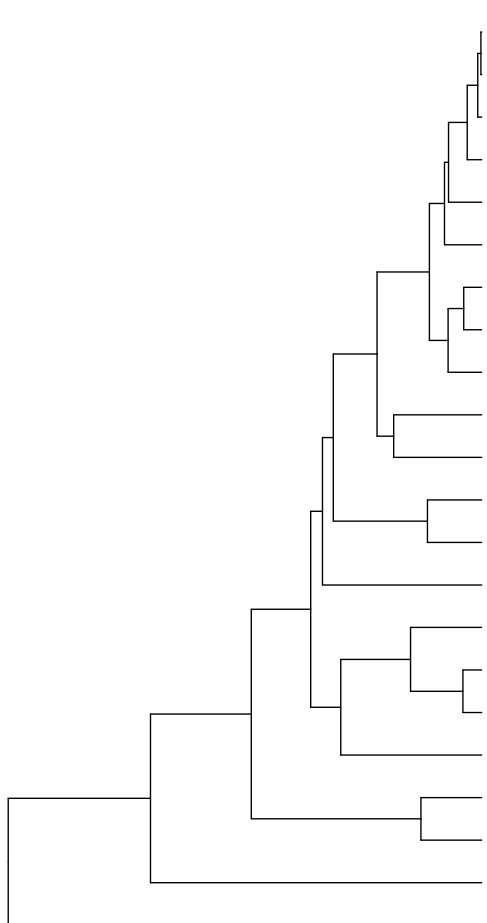
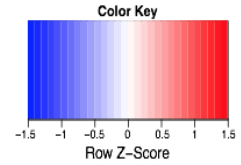
SB414 2% Dose Significantly Changed the Immune Signature of AD Lesions



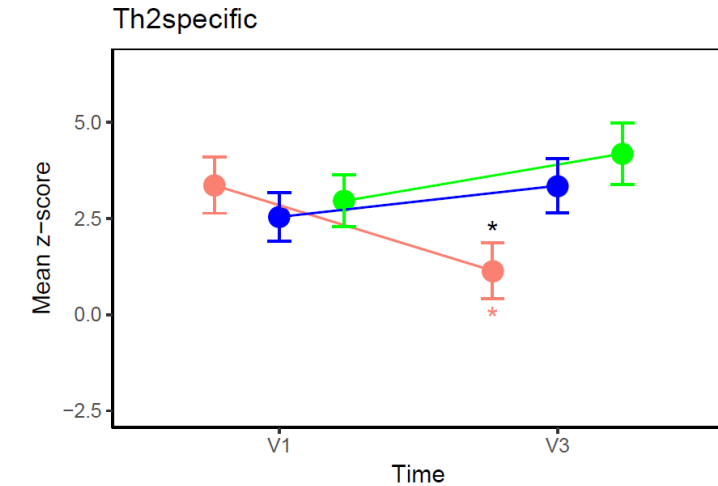
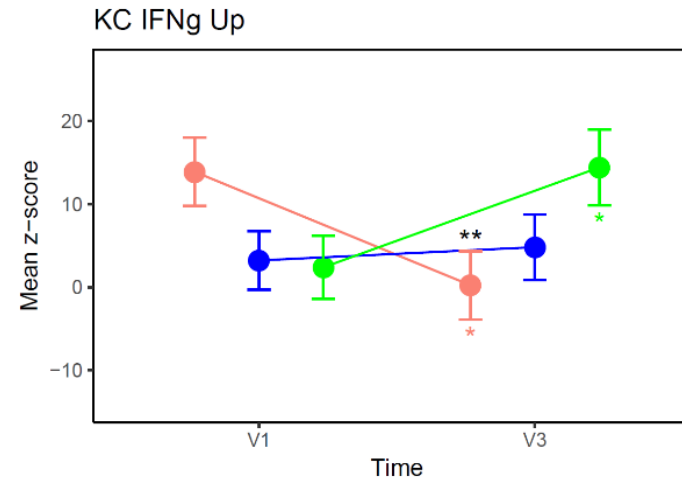
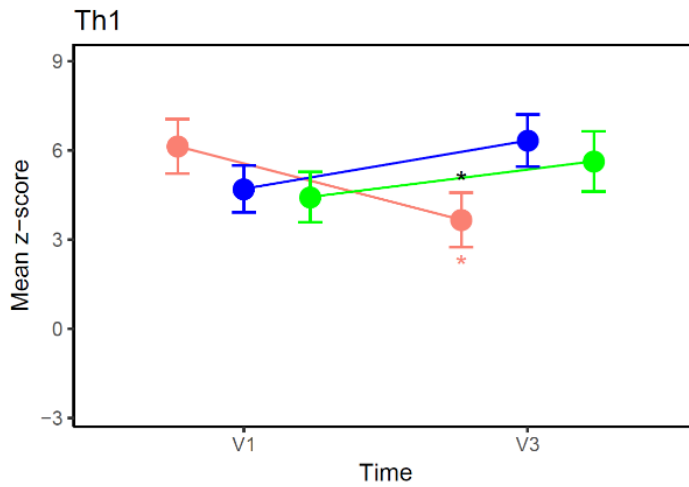
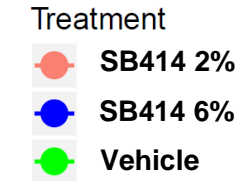
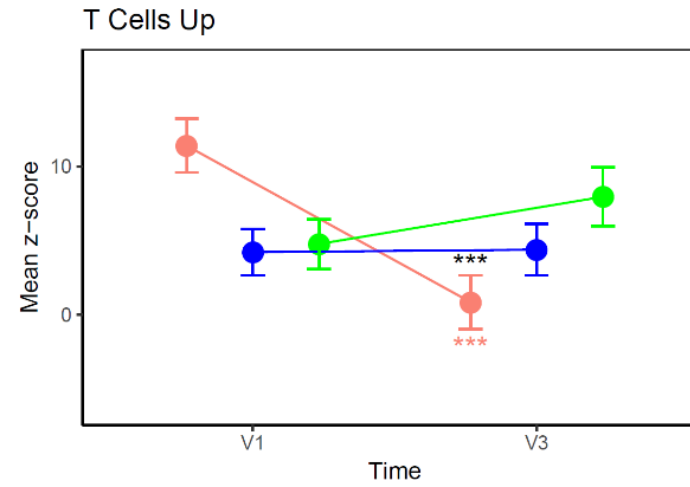
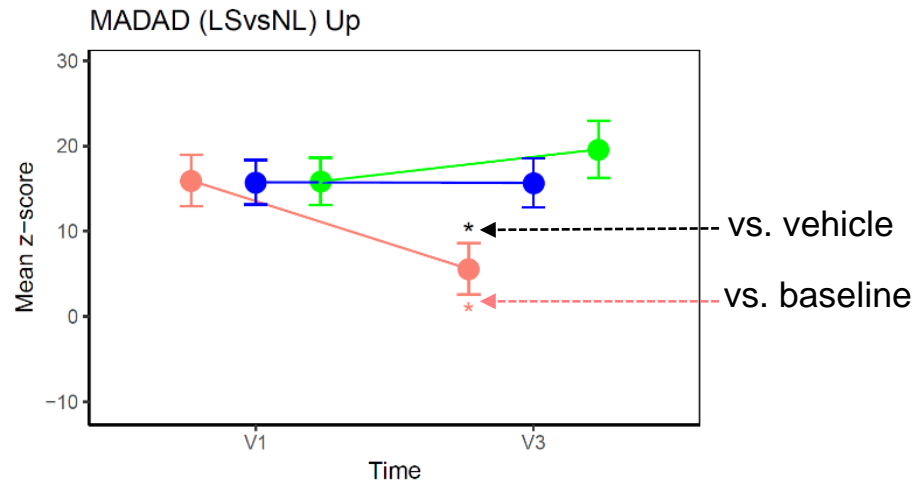
Immune Genes



SB414 2% Dose Significantly Changed the Th17 Gene Pathway of AD Lesions

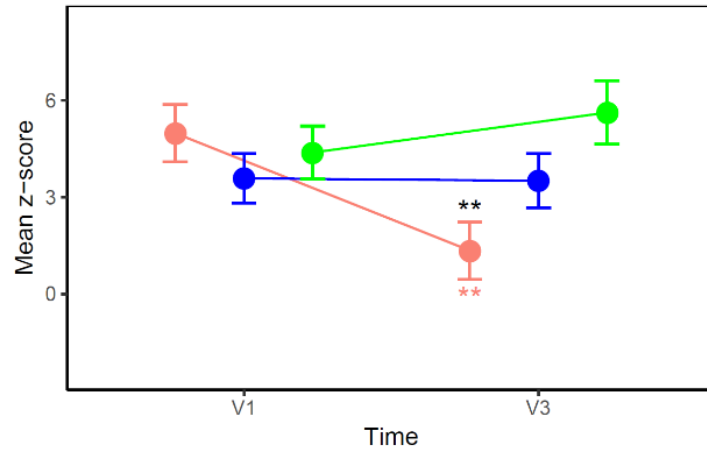


Gene Set Variation Analysis (GSVA): SB414 2% Impacts Additional AD Pathways

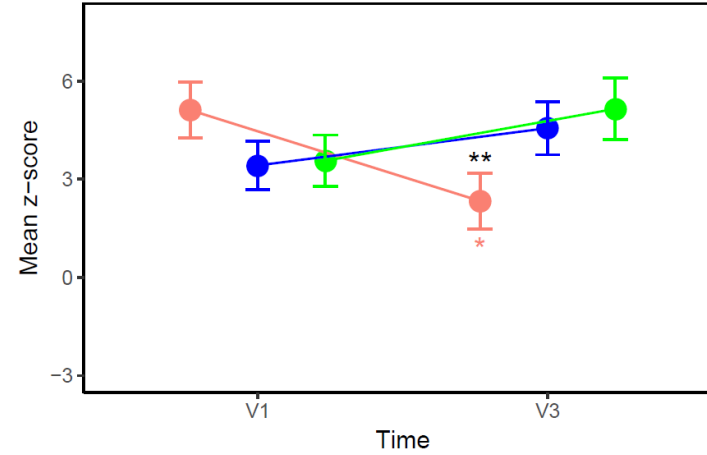


Gene Set Variation Analysis (GSVA): SB414 2% Impacts Additional AD Pathways

KC IL-17 Up

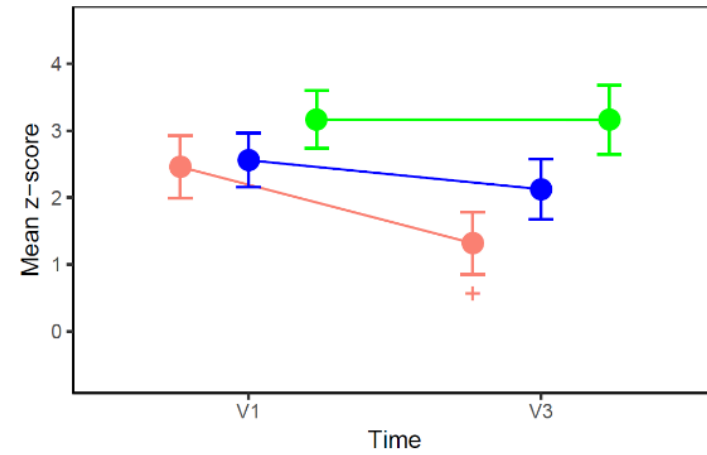


IL-23

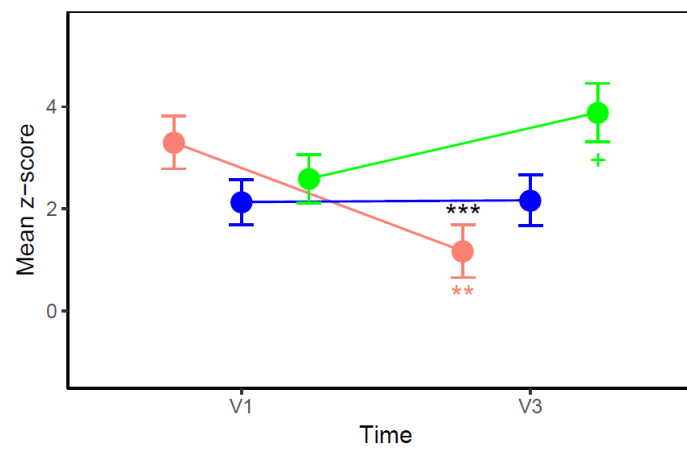


Treatment
● SB414 2%
● SB414 6%
● Vehicle

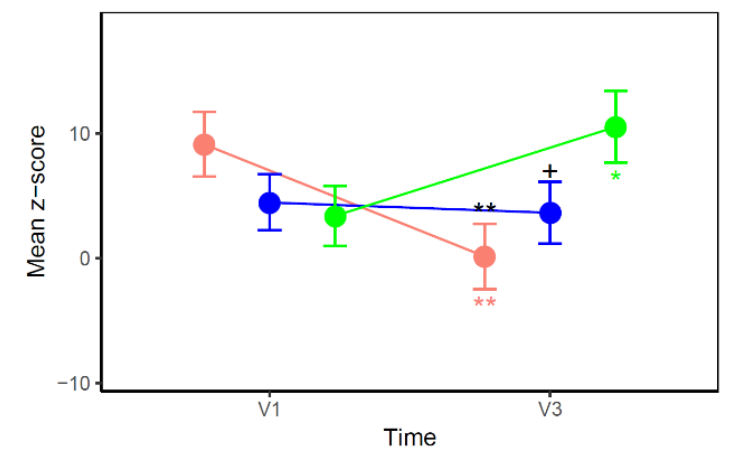
TH22andIL22



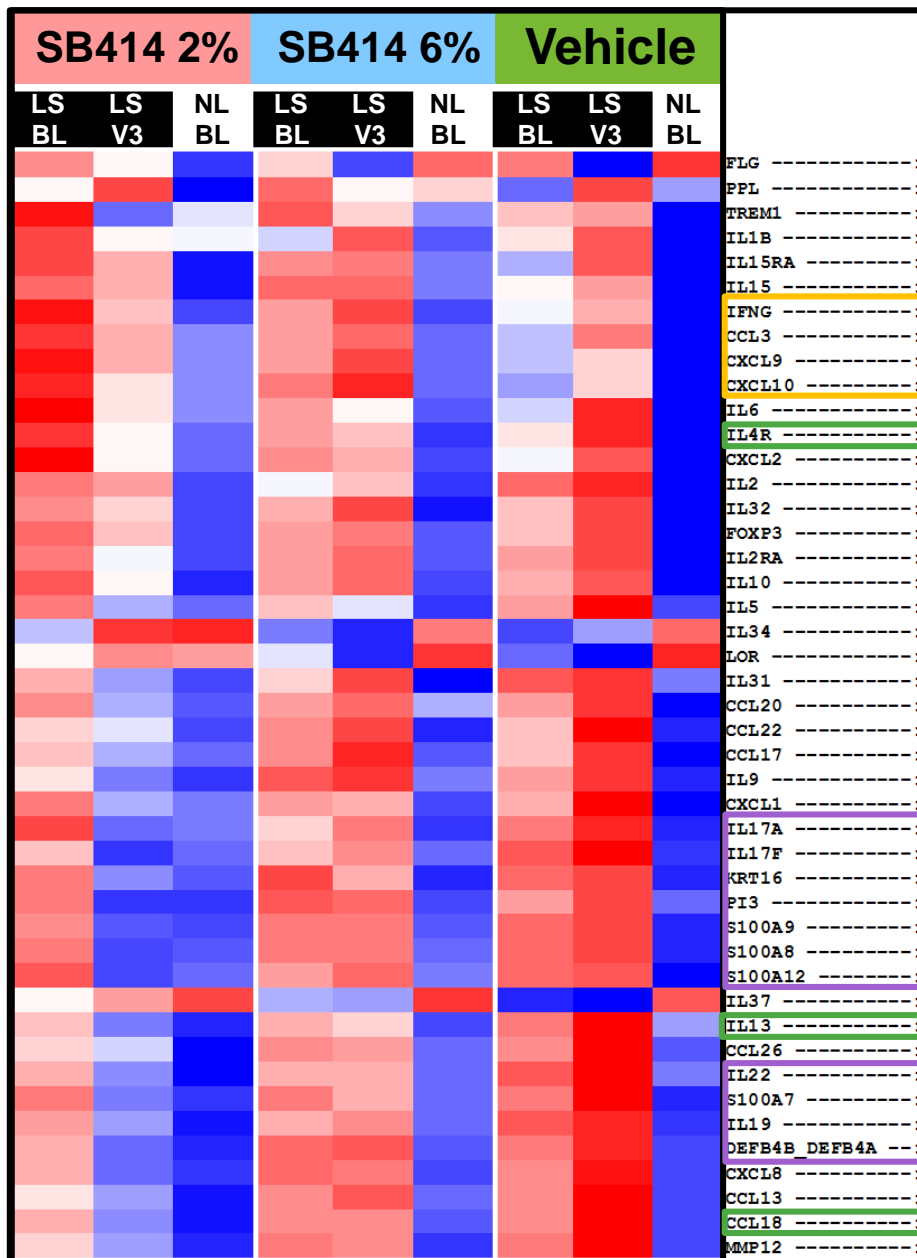
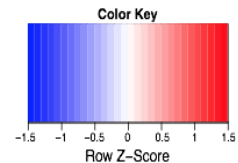
KC IL22 Up



KC TNF Up



RNA-Sequencing Data Validated by RT-PCR

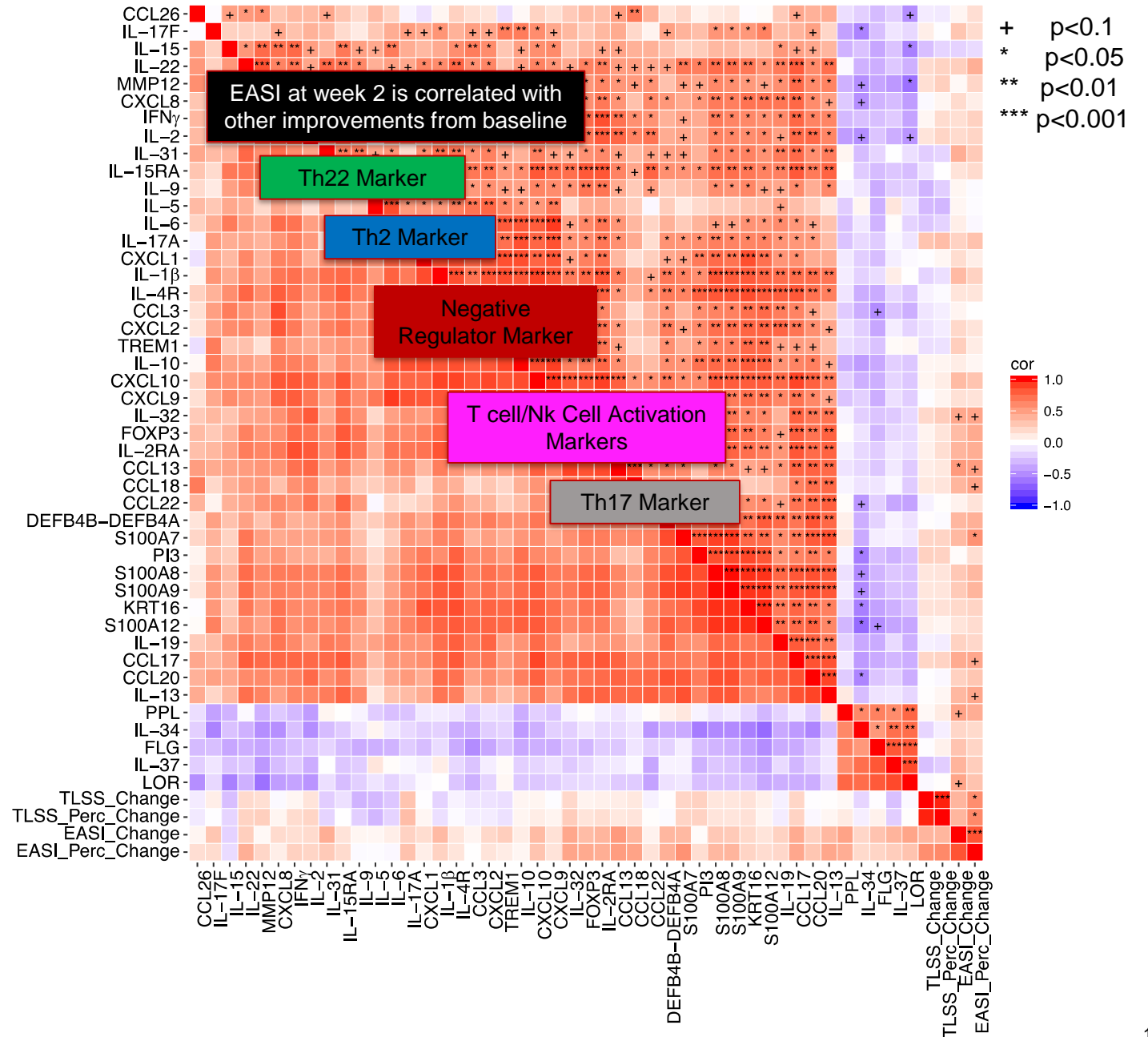


Pathway	Biomarker	2% vs. Veh.	6% vs. Veh.
Th1	IFNG	-3.68*	1.02
	CCL3	-3.46*	-1.77
	CXCL9	-3.63*	-1.09
	CXCL10	-6.02**	-1.26
Th2	IL4R	-2.49**	-1.69+
	IL13	-10.50**	-3.63
	CCL18	-4.47*	-1.94
Th17/Th22	IL17A	-7.41*	-1.01
	IL17F	-7.31*	-1.26
	KRT16	-4.75*	-2.10
	PI3	-11.60***	-1.75
	S100A9	-10.40**	-1.19
	S100A8	-12.70**	-1.40
	S100A12	-13.40**	1.20
	IL22	-7.46*	-1.75
	S100A7	-10.30**	-2.92
	IL19	-6.58	-1.17
	DEFB4B_DEFB4A	-14.00**	-1.92

+ p<0.1; * p<0.05; ** p<0.01; *** p<0.001

Correlations of Biomarker Changes with EASI at Week 2 in SB414 2%

	Correlation	P-Value
EASI_Perc_Change	1.000	0.000
EASI_Change	0.829	0.000
TLSS_Perc_Change	0.602	0.018
TLSS_Change	0.579	0.024
S100A7	0.557	0.034
CCL13	0.507	0.056
CCL18	0.475	0.076
IL32	0.464	0.083
IL13	0.457	0.089
CCL17	0.454	0.092
FOXP3	0.443	0.100
IL2RA	0.421	0.119
IL22	0.414	0.126
DEFB4B.DEFB4A	0.411	0.130



SB414 Summary

- SB414 demonstrated clinical trends suggestive of efficacy in the 2-week study
- 60% improvement in the AD molecular profile was observed with SB414 2%
- Immune pathways significantly changed with treatment with SB414 2% including Th2, Th1 and particularly Th17/Th22
- Significant correlations were seen between skin biomarkers and clinical severity scores