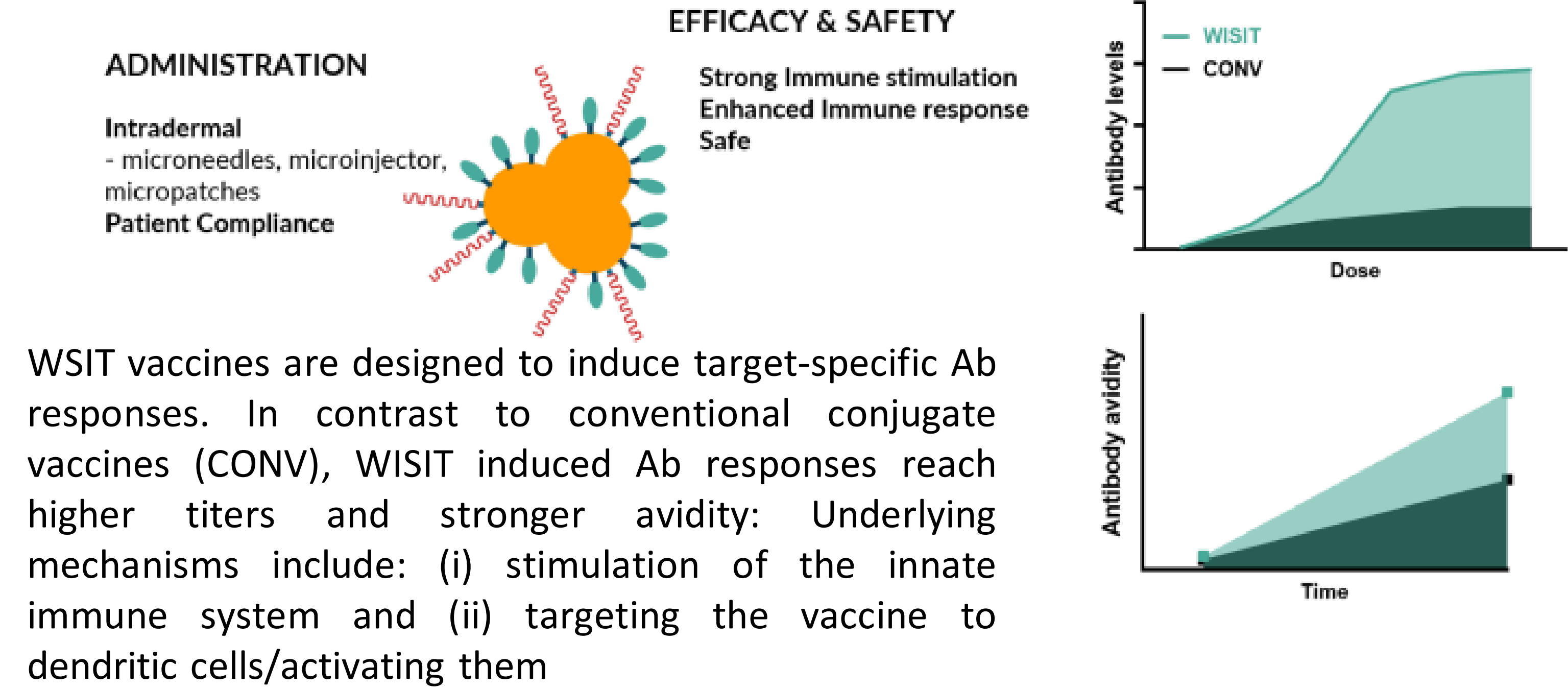


TARGETING CYTOKINES (IL17/23/31) WITH A NOVEL VACCINE FORMAT: IN VIVO POC AND POSITIVE BENCHMARKING TO MARKETING BIOLOGICALS

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BACKGROUND Monoclonal antibodies (Abs) targeting cytokines are commonly used to treat inflammatory skin diseases such as psoriasis and atopic dermatitis. Tridem Bioscience has developed a novel β -glucan-based vaccine platform, termed WISIT (Win the Skin Immune System Trick).

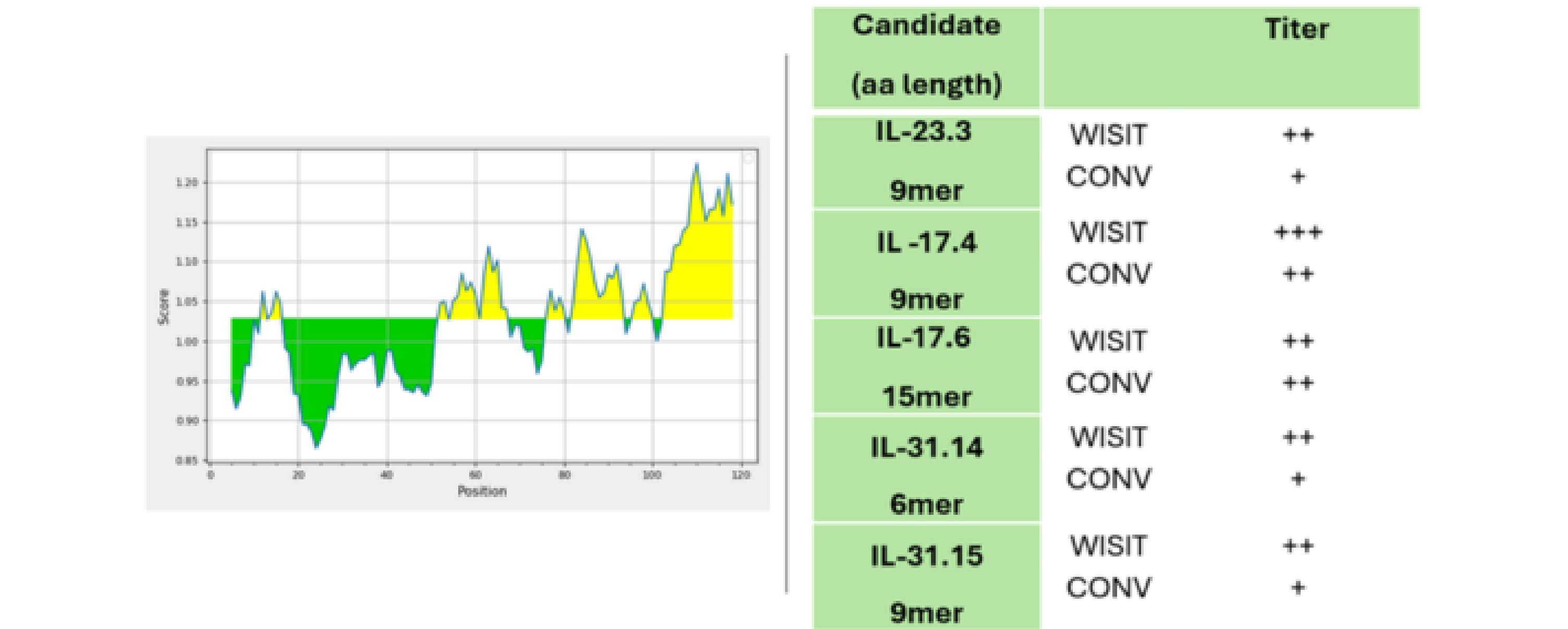


WISIT vaccines are designed to induce target-specific Ab responses. In contrast to conventional conjugate vaccines (CONV), WISIT induced Ab responses reach higher titers and stronger avidity: Underlying mechanisms include: (i) stimulation of the innate immune system and (ii) targeting the vaccine to dendritic cells/activating them

METHODS We identified target regions in cytokines of interest and defined short peptides representing them. These peptides were tested as part of conventional vaccines (peptide/carrier conjugate adsorbed to adjuvant) or WISIT vaccines. Further characterization included benchmarking of WISIT induced Abs to marketed monoclonal Abs (e.g., ixekizumab, bimekizumab, nemolizumab). Top candidates, based on immunogenicity, were assessed in in vitro and in vivo POC studies.

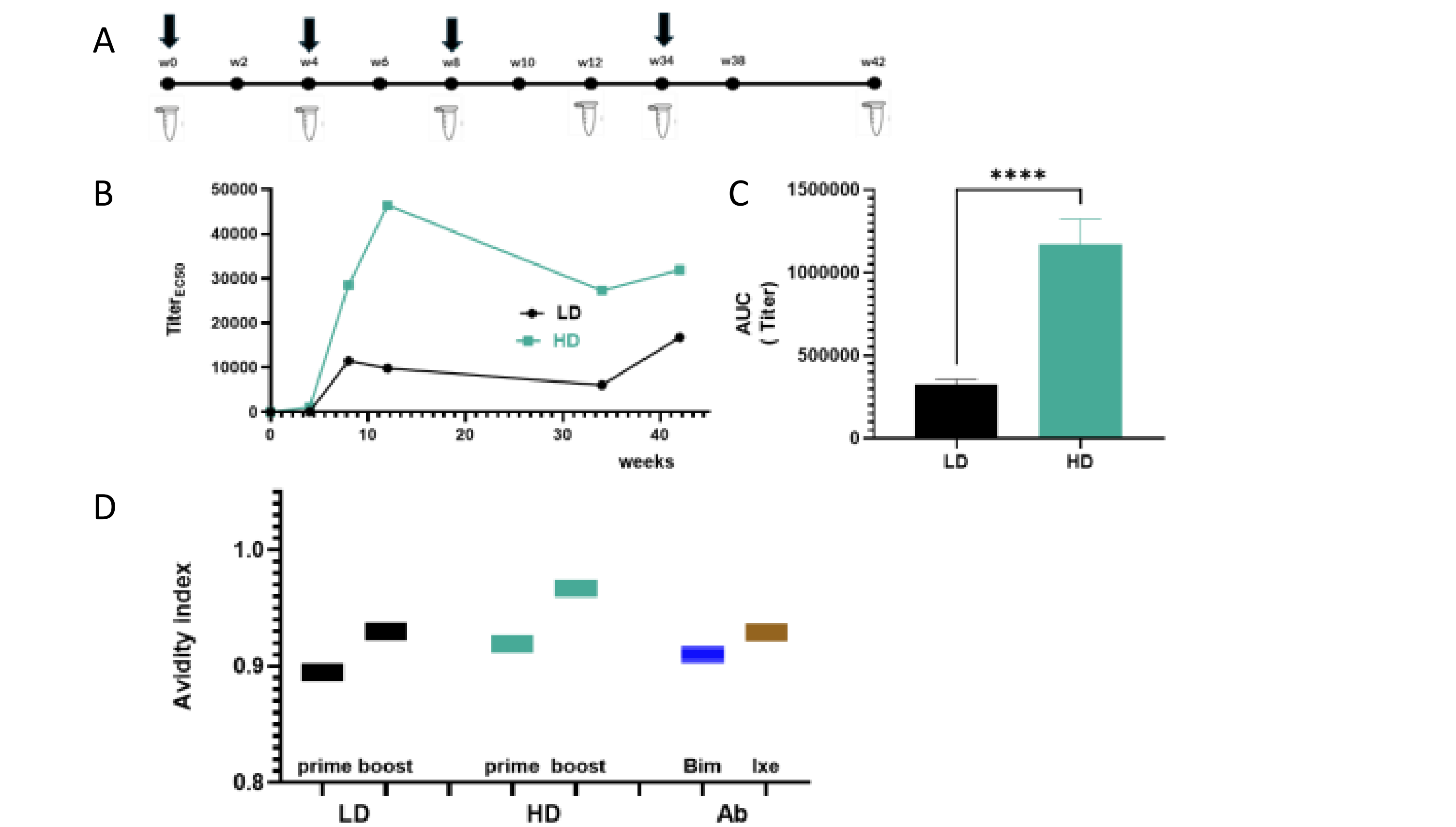
RESULTS

WISIT induces high titer Ab responses to cytokines in mice



BepiPred-3.0 and Kolaskar & Tongaonkar were used for predicting B-cell epitopes and their potential antigenicity (IL-17A as example) and B cell epitopes candidates were screened for reactivity towards the targeted cytokine in Balb/c mice and top candidates were selected for IL17/23/IL31. Titer: : ≥ 400.000 ++; ≥ 200.000 ++; ≤ 100.000 +.

WISIT induces high-avidity, high-titer Ab responses to cytokines in mice



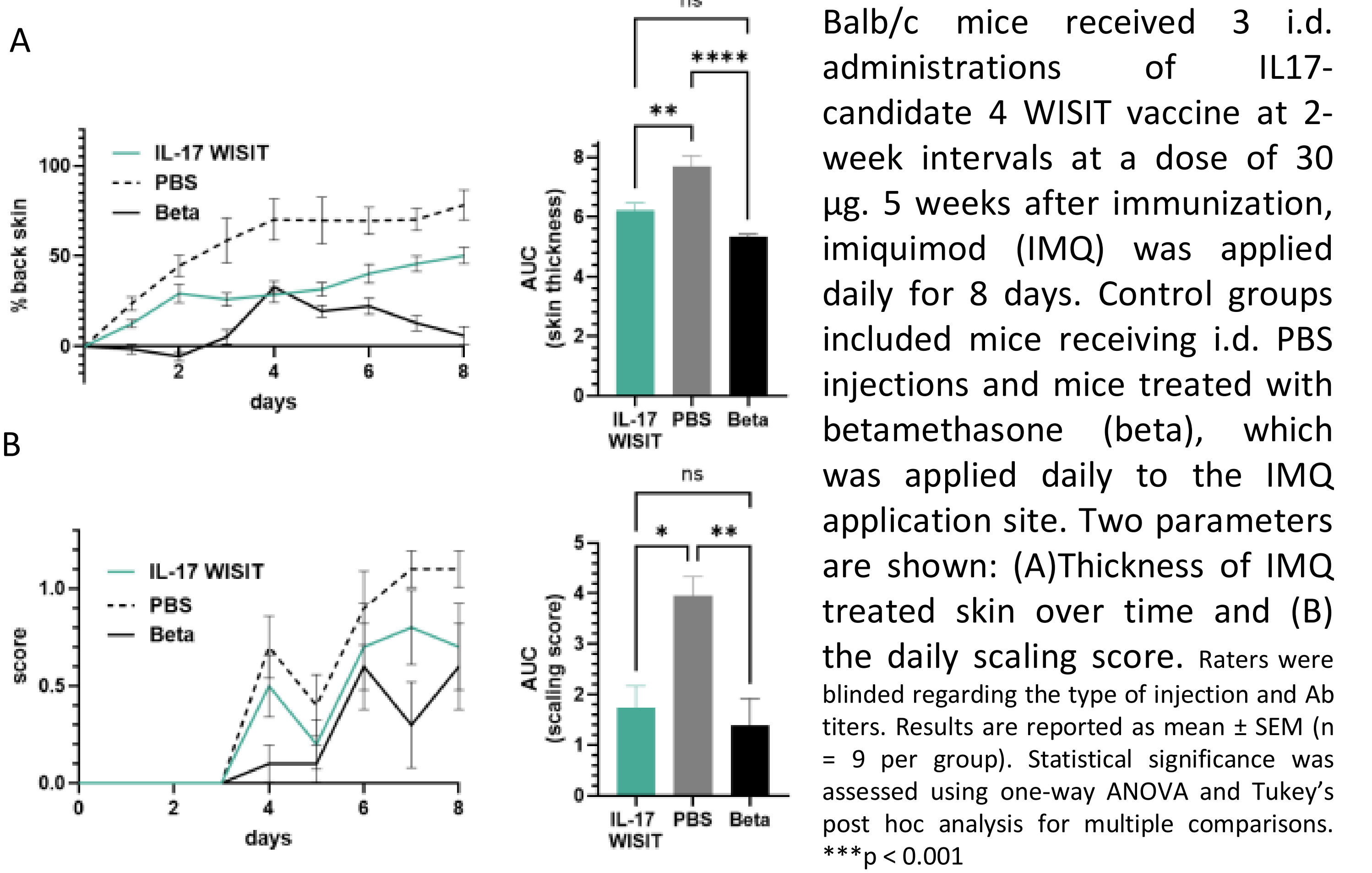
Characterization of the WISIT IL17-induced Ab response. (A) Study design: Female BALB/c mice, aged 8–12 weeks, received 3 intradermal vaccinations at 4-week intervals at 2 doses and a booster at week 34. (B) Ab titer profile and (C) AUC of the low (LD) and high dose (HD) groups. (D) Ab avidity as a function of dose in comparison to bimekizumab (Bim) and ixekizumab (Ixe). The results are reported as mean $\pm$ SEM (n = 10 per group). Statistical significance was assessed using one-way ANOVA and Tukey's post hoc analysis for multiple comparisons. ***p < 0.001.

IL-31 WISIT-induced Abs neutralize IL-31 signaling comparable to nemolizumab

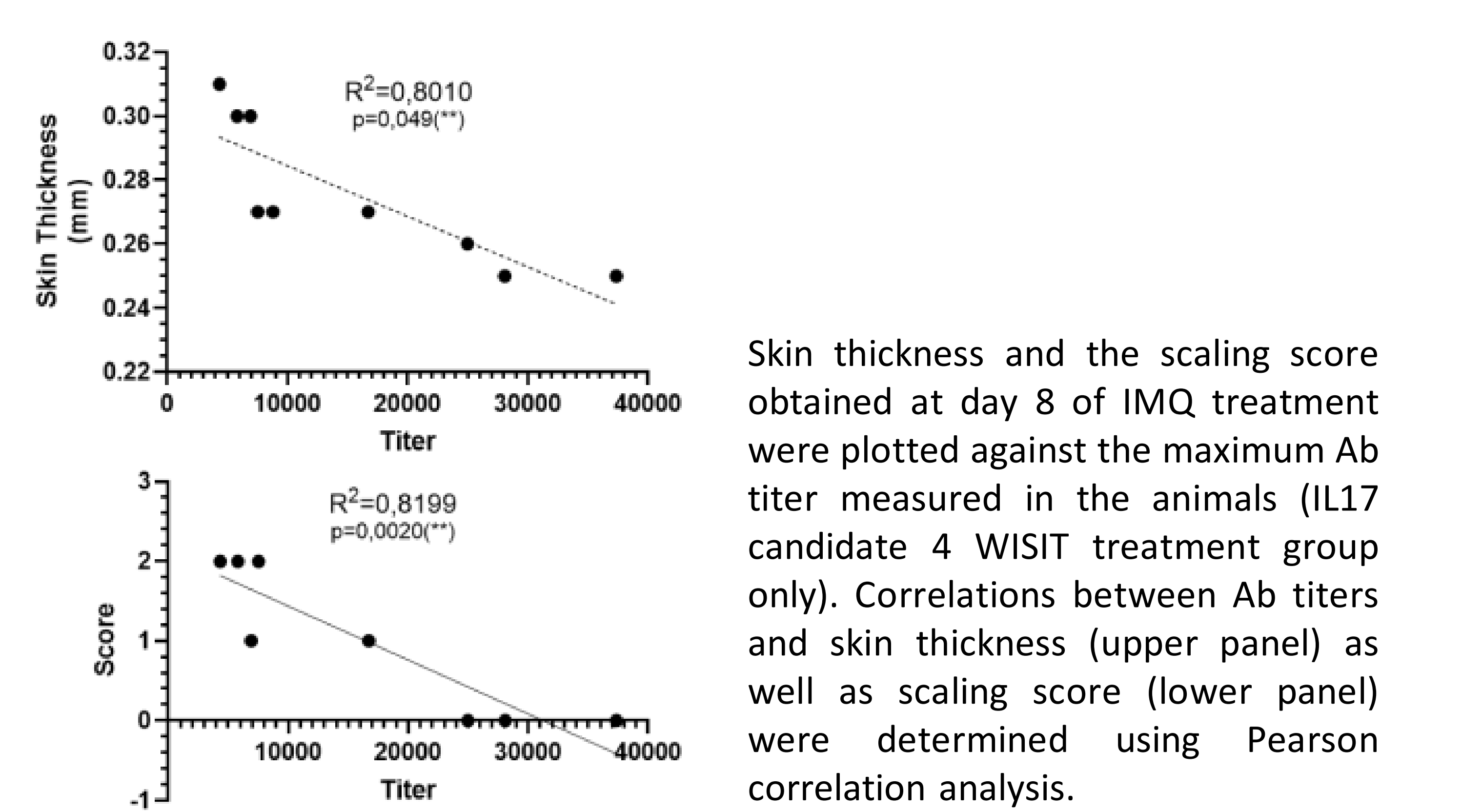
Nemolizumab		IL-31.14	
ng/ml	%Activity	ng/ml	%Activity
1000	8	100	51
250	11		
125	32	IL-31.15	
63	53	ng/ml	%Activity
31	80	100	43
8	100		
0	100		

In vitro POC: Neutralization of hIL-31 signaling as assessed with SEAP assay using HEK-Blue IL-31 reporter cells. Increasing concentrations of nemolizumab or WISIT-induced Abs were incubated with HEK-Blue IL-31 cells for 3 h before the addition of rec. hIL31. After overnight incubation, SEAP activity in the cell culture supernatants was assessed. Data are shown as % of activity for nemolizumab or IL-31 WISIT-induced Abs.

IL-17 WISIT reduces imiquimod-induced psoriatic lesions



Inverse correlation between IMQ-induced disease severity and IL-17 WISIT-induced Ab titers



CONCLUSION These in vivo studies demonstrate that WISIT vaccines can elicit antibodies that react with and inhibit the function of targeted cytokines in an unprecedented manner. They have the potential to create a new, cost-efficient, and sustainable therapeutic approach.

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