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A randomized controlled double blind investigation of the effects of Vitamin D dietary supplementation in subjects with atopic dermatitis

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Abstract

Background—Subjects with atopic dermatitis (AD) have defects in antimicrobial peptide (AMP) production possibly contributing to an increased risk of infections. In laboratory models, vitamin D can alter innate immunity by increasing AMP production.

Objective—To determine if AD severity correlates with baseline vitamin D levels, and to test whether supplementation with oral vitamin D alters AMP production in AD skin.

Methods—This was a multi-center, placebo controlled, double-blind study in 30 subjects with AD, 30 non-atopic subjects, and 16 subjects with psoriasis. Subjects were randomized to receive either 4000 IU of cholecalciferol or placebo for 21 days. At baseline and day 21, levels of 25-hydroxyvitamin D (25OHD), cathelicidin, HBD-3, IL-13, and Eczema Area and Severity Index (EASI) and Rajka-Langeland scores were obtained.

Results—At baseline, 20% of AD subjects had serum 25OHD below 20 ng/ml. Low serum 25OHD correlated with increased Fitzpatrick Skin Type and elevated BMI, but not AD severity. After 21 days of oral cholecalciferol, mean serum 25OHD increased, but there was no significant change in skin cathelicidin, HBD-3, IL-13, or EASI scores.

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The authors have no conflict of interest to declare

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Conclusions—This study illustrated that darker skin types and elevated BMI are important risk factors for vitamin D deficiency in subjects with AD, and highlighted the possibility that seasonality and locale may be potent contributors to cathelicidin induction through their effect on steady state 25OHD levels. Given the molecular links between vitamin D and immune function, further study of vitamin D supplementation in subjects with AD is warranted.

INTRODUCTION

It is hypothesized that AD subjects are susceptible to infections because of multiple deficiencies in the function of their innate immune system, which include defects in the physical epidermal barrier, alteration in pattern recognition receptors, and depression of antimicrobial peptides (AMPs). [1]

AMP expression greatly increases in the skin following infection or wounding, and this induction is comparable to that seen in lesional skin of subjects with psoriasis [2]. However, AD subjects have a relative defect in innate immunity since they express less of some AMPs (cathelicidin, human beta defensin 2 (HBD-2) and human beta defensin 3 (HBD-3), in inflamed skin than expected [3, 4]. This lack of an adequate increase of AMPs in response to skin inflammation may be partially due to a suppressive effect of T helper 2 (Th2) cytokines on the capacity of keratinocytes to express HBD2, HBD-3 and filaggrin [5, 6]. Subjects with AD would benefit from a therapeutic intervention that could normalize their innate immune defense. One potential approach was suggested by observations that cathelicidin expression in humans is induced by 1,25-dihydroxyvitamin D3 (1,25OHD) [7, 8].

Our study sought to examine whether serum vitamin D values correlate with the severity of AD, and whether brief supplementation with oral cholecalciferol could benefit the expression of AMPs in AD skin.

METHODS

Study population

The study population included 30 subjects with AD (mean age of 31.2 years), 30 non-atopic subjects (mean age of 31.9 years), and 16 subjects with psoriasis (mean age of 38.8 years) from San Diego, Denver and Portland. AD subjects had moderate to severe AD with an average Rajka-Langeland score of 6 (ranging from 4 to 9) and psoriatic subjects had mild psoriasis with a mean Psoriasis Area and Severity Index (PASI) of 2.5. Table 1 presents subject's baseline demographics, and Table 2 shows recruitment by locale and seasonality. None of the subjects had received topical corticosteroids, oral or topical antibiotics, oral antivirals, immune enhancers, or topical calcineurin inhibitors for at least one week prior to enrollment. In addition, subjects were excluded from the study if they had received systemic immunosuppressives, chemotherapeutic agents, light therapy, anti-inflammatory biologics, or oral calcineurin inhibitors within 30 days of the baseline visit. All subjects withheld use of these medications for the duration of the study. In addition, any subject taking oral vitamin D or any medication known to interact with calcium or with a history of kidney disease, kidney stones, hyperparathyroidism, sarcoidosis, tuberculosis or lymphoma were excluded from the study.

Study Drug

Vitamin D3 was supplied by the manufacturer, Bio-Tech Pharmacal, Inc. (Fayetteville, AR) and manufactured by S-Heung Capsule Company (Seoul, Korea). Vitamin D was not manufactured specifically for this study. Each capsule contained 4,000 IU vitamin D3. Vitamin D3 was supplied as an off-white powder encapsulated in a clear gelatin capsule. The active ingredient in the vitamin D3 capsule was vitamin D3 powder (quantity 8% by weight). Inactive ingredients included Vivapur® type 101 cellulose (microcrystalline cellulose, quantity 84% by weight) and Cab-O-Sil M5 (fumed silica, quantity 8% by weight).

Study Design

All subjects were randomized 1:1 to receive either placebo or active Vitamin D through a centralized randomization system. Subjects were instructed to take one capsule per day. Vitamin D3 capsules were from lots 6403 and 6825. Blinded labels were affixed to the tinted containers containing either placebo or vitamin D3 capsules.

At baseline, serum calcium, creatinine, parathyroid hormone (PTH), IgE and 25-hydroxyvitamin D (25OHD) levels were obtained. Punch biopsies of skin were performed with 2 mm samples obtained from uninvolved skin of all subjects. AD and psoriatic subjects also received 2 mm punch biopsies of lesional skin at least 2 cm from the uninvolved site. The skin samples were immediately flash frozen in TRIzol® (Invitrogen, Carlsbad, CA) and stored at –80°C for RNA extraction and qRT-PCR. At 21 days, all subjects returned for repeat 2 mm skin biopsies of uninvolved skin in an area at least 2 cm from the previous biopsy, as well as repeat serum calcium, creatinine, PTH, IgE and 25OHD levels. AD and psoriatic subjects also received a 2 mm punch of involved skin in an area at least 2 cm from the initial biopsy site. The study was submitted under an investigational new drug (IND) application and approved by the Human Research Protection Program at the University of California San Diego; the Institutional Review Boards at National Jewish Health Center and Oregon Health and Science University; and the NIAID Allergy and Asthma Data Safety and Monitoring Board (DSMB). The study was registered with [ClinicalTrials.gov](https://clinicaltrials.gov) on 11/11/08, (#NCT00789880), and the first subject enrolled on 1/7/09. All subjects gave written informed consent.

Quantification of Cathelicidin, IL-13, and HBD-3 in Skin

Analysis of cathelicidin, *IL13* (IL-13 gene), and *DEFB103A* (HBD-3; human *b*-defensin-3 gene) expression in skin was performed by qRT-PCR. Total RNA was isolated from the 2 mm skin biopsy samples. Briefly, the biopsy samples were placed into 2.0 ml polypropylene tubes (Biospec Products, Bartlesville, OK) with 1.0 ml Trizol (Invitrogen Corp, Carlsbad, CA). Zirconia/Silica beads (Biospec Products) were added to the tubes and the skin samples were then homogenized using a Mini-beadbeater-8 (Biospec Products). Homogenized Trizol solution was transferred to RNase free tubes for RNA extraction according to the manufacturer's instructions. cDNA was synthesized from RNA by the iScript cDNA Synthesis Kit (BioRad, Munchen, Germany). Real-time qRT-PCR assay for cathelicidin was performed with the ABI 7000 Sequence Detection system (PE Applied Bio systems, Foster City, CA). Expression of cathelicidin was evaluated by using a FAM-

CAGAGGATTGTGACTTCA-MGB probe with primers 5'-CTTCACCAGCCCGTCCTTC-3' and 5'-CCAGGACGACACAGCAGTCA-3'. TaqMan Gene Expression Assays (Applied Biosystems) were used to analyze expression of *IL-13* (assay ID: Hs00174379_m1) and *DEFB103A* (assay ID: Hs00218678_m1) with the use of the ABI 7000 Sequence Detection system (Applied Bio systems). *GAPDH* mRNA was used as an internal control to normalize RNA for each sample. For *GAPDH* expression, a VIC-CATCCATGACAACCTTTGGTA-MGB probe with primers 5'-CTTAGCACCCCTGGCCAAG-3' and 5'-TGGTCATGAGTCCTTCCACG-3' were used. Fold induction was calculated using the 2-delta cycle threshold (CT) method, where delta CT is the CT of target genes minus the CT of *GAPDH*, and CT is the cycle at which an arbitrary detection threshold is crossed (refer to user bulletin #2 by Applied Biosystems). Cathelicidin, *IL-13*, and *DEFB103A* mRNA were calculated as the relative expression to *GAPDH* mRNA, and all data are presented as normalized data against each control.

Statistical Analysis

A sample size of 30 AD subjects (and 30 non-atopic controls) was chosen to provide at least 82% power to detect a difference in the change in expression of cathelicidin of 3.3 cycles (with an assumed variance of 9.0 cycles) between vitamin D3 and placebo treated subjects. An additional 16 psoriatic subjects were chosen for exploratory purposes based on similar assumptions as above and an anticipated half-width of approximately 2.1 cycles for 95% confidence intervals. Comparisons at baseline between groups were made using a two-sample t-test for continuous variables and a Chi-square test for categorical variables. Relationships between continuous variables were quantified using a Pearson correlation coefficient with the associated test. When required, variables were log transformed for analysis (e.g. IgE). Comparisons of cathelicidin, HBD-3, and IL-13 at baseline, day 21, and change from baseline were made between vitamin D3 versus placebo in AD, psoriatic, and non-atopic control subjects (separately) using a 2-sided independent sample t-test. Separate comparisons were made for lesional skin, non-lesional skin, and the difference between the two (lesional minus non-lesional skin). Cathelicidin, HBD-3, and IL-13 were then compared across the three diagnostic groups using analysis of variance (ANOVA) techniques. Since these comparisons were descriptive and exploratory, no adjustments were made for multiple comparisons.

RESULTS

We examined a total of 76 subjects: 30 with AD, 30 non-atopic controls, and 16 subjects with psoriasis. There were no significant differences at baseline among the diagnostic groups in terms of age, gender, race, ethnicity, body mass index (BMI), serum calcium, PTH, or creatinine (Table 1). Serum IgE at baseline was significantly increased in the AD subjects compared to non-atopic controls or psoriatics ($p < 0.01$) (Table 1). AD subjects had a mean baseline serum 25OHD level of 28.4 ng/ml. No significant differences in serum 25OHD existed among subjects with AD, psoriasis, or non-atopic controls. At baseline, 57% of the AD subjects had 25OHD levels below 30ng/ml and 20% had levels below 20ng/ml, a level that represents vitamin D deficiency as recently established by the IOM [9]. Categorized by Fitzpatrick Skin Type, AD subjects with Type V/VI skin had a significantly

lower mean 25OHD level of 18.8 ng/ml in comparison to Type III/IV with a mean 25OHD level of 28.7 ng/ml ($p=0.04$, Fig. 1). Also in AD subjects, serum 25OHD levels were inversely correlated with body mass index (BMI) ($r=-0.38$, $p=0.04$); i.e., lower 25OHD levels were observed with higher BMIs (Fig. 2A). There was no correlation between baseline 25OHD levels and baseline Rajka-Langeland scores (Fig. 2B).

Consistent with the literature, relative abundance of cathelicidin and HBD-3 mRNA at baseline was significantly higher in lesional psoriatic skin compared to the skin of non-atopic controls ($p<0.01$ and $p<0.01$, respectively; Figs. 3A/B). Also, relative abundance of HBD-3 mRNA was significantly lower in AD lesional skin compared to psoriatic lesional skin ($p<0.01$; Fig. 3B), reflecting the diminished innate immune defense capacity of these subjects. For cathelicidin, there was no statistically significant difference between AD lesional skin, AD non-lesional skin, and the skin of non-atopic controls. For HBD-3, levels were greater in AD lesional skin compared to AD non-lesional skin and the skin of non-atopic controls ($p<0.01$ and $p<0.01$, respectively; Fig. 3B). This finding reinforces previous observations that it is a defect in the relative increase of cathelicidin and β -defensins in comparison to psoriatics rather than an absolute decrease or absence of AMP expression. In addition, relative abundance of IL-13 mRNA levels were increased in AD lesional and non-lesional skin compared to the skin of non-atopic controls ($p=0.01$ and $p=0.02$, respectively; Fig. 3C).

After three weeks of supplementation with 4000IU of vitamin D3, serum 25OHD levels significantly rose in non-atopic controls from a mean at screening of 30.1 ng/mL to 39.5 ng/mL ($p<0.01$) and in atopic subjects from a mean of 28.4 ng/mL to 37.8 ng/mL ($p<0.01$); serum 25OHD levels did not significantly rise in psoriatic subjects ($p=0.18$, Fig. 5). Subjects receiving placebo showed no significant change in serum 25OHD (data not shown). AD subjects with lower levels of 25OHD at screening had the largest change in serum vitamin D levels after three weeks of supplementation ($r=-0.77$, $p<0.01$, Fig. 6A). The non-atopic controls and psoriatic subjects did not exhibit this association ($r=-0.01$, $p=0.99$; $r=-0.50$, $p=0.21$, respectively). Serum calcium, IgE, and PTH did not change significantly with vitamin D supplementation or with placebo (data not shown). Five adverse events (AEs) were reported during this study; none of which were serious or determined to be related to the therapy.

Under these conditions, we did not observe a change in skin cathelicidin or HBD-3 mRNA in any diagnostic groups in either lesional or non-lesional skin after oral vitamin D3 supplementation (Fig. 4) in AD subjects. Placebo subjects also showed no change (supplemental data). Interestingly however, when broken out by site, Portland's subjects had statistically significant lower levels of cathelicidin when compared to San Diego and Denver both at day 0 and day 21 ($p=0.006$, $p=0.001$, Fig. 7A). Examination of vitamin D levels separated out by site revealed that AD subjects from Portland also had a significantly lower level of vitamin D at day 0 (Fig. 7B), controlling for Fitzpatrick skin type.

Finally, no significant correlation was observed between the changes in vitamin D versus the change in expression of IL-13 in AD subjects' lesional skin. Non-atopic controls and subjects receiving placebo also showed no significant change in expression of these AMPs.

However, AD subjects had a weak negative correlation indicating that less change in IL-13 mRNA expression in lesional skin may be associated with a higher change in 25OHD ($r = -0.36$, $p = 0.06$, Fig. 6B). No change in mean EASI or PASI was seen following supplementation.

DISCUSSION

Vitamin D deficiency has been suggested to be associated with increased rates of many cancers, as well as autoimmune and cardiovascular disease [10–12], asthma [13], innate and adaptive immune functions [14, 15] and epithelial growth and differentiation [16]. The present study was designed to test the hypothesis that dietary vitamin D might benefit the innate immune function of AD skin, since in-vitro evidence has demonstrated that vitamin D can induce AMPs in cultured human cells [17], and that mice deficient in the vitamin D receptor have abnormal barrier function, lipid secretion and composition [18]. In this short trial, we did not find that supplementation with oral vitamin D influenced AMP expression in AD. However, we did uncover a high rate of vitamin D deficiency in all subject populations, illustrated variables that influence the response to oral vitamin D, and found a promising potential towards decreasing TH2 cytokine expression with increasing serum vitamin D levels.

In our study, neither the baseline EASI scores in ADs or baseline PASI scores in psoriatics were associated with serum 25OHD levels. Other studies in the literature have found a correlation between vitamin D levels and AD severity [19], while others have not [20]. Similarly, supplementation studies have shown modest improvement in EASI and Investigator's Global Assessment (IGA), which did not reach statistical significance [21], while other supplementation trials have shown improvement with (Scoring Atopic Dermatitis) SCORAD [22, 23]. Given the small size of this study, and the variability in the results of previous studies, further work is necessary to rule out this lack of correlation.

Several factors influence vitamin D status, and our study confirmed that these factors also influence vitamin D status in AD subjects. Dark-skinned individuals with Fitzpatrick Skin Types V/VI had lower levels of 25OHD in comparison to Types III/IV ($p = 0.04$). Also consistent with prior literature on vitamin D, we observed lower 25OHD levels in subjects with higher BMI [24]. This negative influence has been suggested to be due to the lipophilic nature of vitamin D and distribution into the increased stored fat in subjects with high BMI [25].

We also observed a significant overall change in serum 25OHD levels following oral supplementation with vitamin D in AD and non-atopic control subjects, but not in psoriatics ($p < 0.01$, $p < 0.01$, and $p = 0.18$, respectively). The lack of an increase in serum 25OHD levels in subjects with psoriasis may be due to an increased BMI in this group (Table 1), which although not statistically significant, does concur with prior studies that have shown higher BMI to be associated with lower vitamin D levels [25]. Our study revealed that AD subjects with lower baseline vitamin D levels had a larger increase in vitamin D following supplementation. This finding has been reported previously in healthy individuals [26], but not in subjects with AD.

Despite an increase in 25OHD levels seen here in most subjects, there was no statistically significant correlation between the change in vitamin D and a change in abundance of cathelicidin or HBD-3. There have been similar studies that both agree with and refute this finding. In a similar study published recently, subjects treated with 15 narrow band UVB treatments had a significant increase in vitamin D levels, but similar to our study had no statistically significant increase in cathelicidin production in atopic lesions²⁰. Contradicting this finding, is a smaller study from our group that demonstrated an increase in cathelicidin production in the lesional skin of AD subjects after vitamin D supplementation [27]. In our original single site study, we also supplemented with oral vitamin D at identical doses and duration although the manufacturer differed between the two studies (Biotech Pharmacal, Fayetteville, AR, versus Leader®, Cardinal Health, Dublin, Ohio). Further examination of our previous study also revealed that supplementation primarily took place in the winter months (71%) in San Diego, in contrast to 20% in the winter in our current multi-center study. In addition, we noted that there were significant baseline vitamin D and cathelicidin differences between the three sites (Portland, Denver and San Diego), which may have further confounded our results. Interestingly, Portland subjects had significantly lower baseline vitamin D levels and cathelicidin levels in comparison to Denver and San Diego. The AD subjects from Portland were also recruited primarily in the spring (87%), while Denver's were primarily in the summer (62%), and UCSD was mainly in the summer (47%) and winter (33%) (Table 2). If cathelicidin responds in some way to a steady state concentration of vitamin D, then seasonality may have affected our results, making short-term supplementation ineffective in its ability to increase cathelicidin levels. Thus, in our effort to increase our sample size and power of our study, we may have inadvertently introduced more variability, making it more difficult to interpret our current data. Finally, a recent finding has shown that cathelicidin expression is also controlled by PTH which will increase under conditions of low vitamin D [28]. Thus, the PTH response in different patient cohorts may confound interpretations of cathelicidin expression based only on serum 25OH vitamin D. Further work is thus necessary to draw a definitive conclusion regarding the effectiveness of this approach.

Finally, a weak negative, correlation was observed here between the change in vitamin D and the change in expression of IL-13 mRNA in AD lesional skin ($r=-0.36$, $p=0.06$). IL-13 and other Th2 cytokines are a critical element of the pathophysiology of AD and can lead to suppression of AMPs. However, due to the small sample size, varying seasonality, locales, skin types, and short duration of treatment, our study could not conclude that supplementation with oral vitamin D will alter Th2 cytokine production. The ability to alter this phenotype would be a powerful tool to improve the clinical presentation of many with AD. Thus, further investigations of an association between Th2 cytokines and vitamin D nutritional status are also warranted.

In summary, this study illustrated that darker skin types and elevated BMI are important risk factors for vitamin D deficiency in subjects with atopic dermatitis. It also highlighted the possibility that seasonality and locale may be potent contributors to cathelicidin induction through their effect on steady state 25OHD levels. Given the molecular links between vitamin D and immune function, further study of vitamin D supplementation in subjects with atopic dermatitis is warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

1,25OHD	1,25-dihydroxyvitamin D ₃
25OHD	25-hydroxyvitamin D
ANOVA	Analysis of variance
AMP	Antimicrobial peptides
AD	Atopic dermatitis
BMI	Body mass index
CT	Cycle threshold
DSMB	Data Safety and Monitoring Board
EASI	Eczema Area and Severity Index
HSV	Herpes simplex virus
HBD-2	Human beta defensin 2
HBD-3	Human beta defensin 3
IND	Investigational new drug
IGA	Investigator's Global Assessment
IOM	Institute of Medicine
PTH	Parathyroid hormone
PASI	Psoriasis Area and Severity Index
qRT-PCR	Quantitative reverse-transcriptase polymerase chain reaction
SCORAD	Scoring Atopic Dermatitis
Th1	T helper 1
Th2	T helper 2
TGF-β	Transforming growth factor beta

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Figure 1. Association of baseline serum 25OH vitamin D levels with skin pigmentation, body mass index and atopic disease severity

Atopic Dermatitis subjects with darkest skin pigmentation as measured at Fitzpatrick Skin

Type V/VI had significantly lower serum 25OH vitamin D levels (mean= 18.8 ng/ml)

compared to Type III/IV (mean= 28.7 ng/ml; $p=0.04$).

Figure 2. Association of baseline serum 25OH vitamin D levels with body mass index and atopic disease severity

A: Scatterplot of serum 25OH vitamin D levels versus body mass index (BMI) showed a significant negative correlation ($r=-0.38$, $p=0.04$) with lower vitamin D levels associated with higher BMI. **B:** Scatterplot of baseline 25OH vitamin D levels versus atopic disease severity as measured by Rajka-Langland scores showed no correlation ($r=0.04$, $p=0.85$).

Figure 3. Baseline relative abundance of cathelicidin, HBD-3 and IL-13 mRNA in lesional and non-lesional skin in subjects with atopic dermatitis and psoriasis

A: Cathelicidin gene (*CAMP*) mRNA expression from skin biopsies as measured by qRT-PCR in lesional (L) and non-lesional (NL) skin of atopics (AD), psoriatics (Psor) and skin of non-atopic (NA) control subjects. **B:** Human beta-defensin-3 (HBD-3) mRNA expression from skin biopsies as determined in figure 2A. **C:** Interleukin-13 (IL-13) mRNA expression from skin biopsies as determined in figure 2A. All data are normalized to expression of GAPDH mRNA and mean value determined for NA skin. Both cathelicidin and HBD-3 levels were significantly higher in lesional psoriatic skin compared to controls ($p<0.01$ and $p<0.01$, respectively), and HBD-3 in AD lesional skin was significantly lower than lesional skin in psoriatics ($p<0.01$). IL-13 levels were higher in AD lesional and non-lesional skin compared to controls ($p=0.01$ and $p=0.02$, respectively).

Figure 4. Cathelicidin and HBD-3 mRNA abundance in lesional skin by diagnostic group at screening and after 21 days of oral vitamin D3

A: Cathelicidin (CAMP) mRNA measured as in Figure 2 at initial study screening (Scr) visit and after 21 days of supplementation with oral vitamin D3 at 4000IU/day (21) in subjects with atopic dermatitis (AD) and Psoriasis receiving active oral vitamin D. **B:** Human beta-defensin-3 (HBD-3) mRNA measured as in A. All data are normalized to expression of GAPDH mRNA and mean value determined for non-atopic control skin. Box plot data are shown with median, mean (+), upper and lower quartiles, minimum value and maximum value. Data showed no significant change in the means following supplementation. AD subjects (n=15), Psoriasis subjects (n=8)

Figure 5. Vitamin D serum 25OHD levels by diagnostic group at screening and after 21 days of oral vitamin D3

Serum 25OH vitamin D measured at initial study screening (Scr) visit and after 21 days of supplementation with oral vitamin D3 at 4000IU/day (21) for subjects receiving actual oral vitamin D. Box plot data are shown with median, mean (+), upper and lower quartiles, minimum value and maximum value. Data showed a significant increase in serum vitamin D levels in AD and non-atopic (NA) control subjects after 21 days of vitamin D supplementation ($p < 0.01$ and $p < 0.01$ respectively). Psoriasis subjects did not show a significant increase. AD (n=14), Psoriasis (n=8), Non-AD (n=15).

Figure 6. Relationship between the change in lesional IL-13 mRNA and change in 25OHD after 21 days of oral vitamin D3

A: Scatterplot of screening serum 25OHD levels (ng/ml) versus change in 25OHD from screening after the end of supplementation showed that AD subjects with the lowest vitamin D levels had the greatest increase in vitamin D ($r = -0.77$, $p < 0.01$). The non-atopic controls and psoriatic subjects did not exhibit the same association. **B)** Scatterplot of change in serum 25OHD versus change in log relative abundance of IL-13 mRNA in AD lesional skin measured by qPCR as described in Figure 2. A weak trend was observed for decreasing change in IL-13 with increasing change in serum 25OHD ($r = -0.36$, $p = 0.06$).

Figure 7. Baseline cathelicidin mRNA and serum 25OHD distinguished by site

A: Cathelicidin mRNA measured at initial study screening (Scr) visit and after 21 days of supplementation in subjects with AD (n=15) and Psoriasis (n=8) receiving active oral vitamin D stratified by site. Data is normalized to GAPDH mRNA and mean value determined from non-atopic control skin. Portland had a statistically significant decrease in cathelicidin when compared to San Diego and Denver both at day 0 and day 21 (*p=0.006, ** p=0.001) **B:** We then compared baseline 25OHD in Portland as compared to the San Diego and Denver sites. Portland subjects (mean = 23.7 ng/mL) showed a significantly lower 25OHD level as compared to the other sites (mean=32.8 ng/mL) at baseline, controlling for Fitzpatrick skin type (p=0.0287).

Table 1

Demographic Characteristics

	Diagnostic Group			
	AD N=30	Psoriasis N=16	NA N=30	Total N=76
Gender - n (%)				
Female	16 (53.3%)	8 (50.0%)	17 (56.7%)	41 (53.9%)
Age (years)				
Mean (SD)	31.2 (10.49)	38.8 (11.23)	31.9 (10.86)	33.05 (11.06)
Race - n (%)				
African American	5 (16.7%)	0 (0.0%)	3 (10.0%)	8 (10.5%)
Caucasian	17 (56.7%)	11 (68.8%)	22 (73.3%)	50 (65.8%)
Other	8 (26.7%)	5 (31.3%)	5 (16.7%)	18 (23.7%)
Ethnicity - n (%)				
Hispanic or Latino	1 (3.3%)	2 (12.5%)	6 (20.0%)	9 (11.8%)
Fitzpatrick Skin Scale - n (%)				
Types I/II	6 (20.0%)	6 (37.5%)	9 (30.0%)	21 (27.6%)
Types III/IV	19 (63.3%)	9 (56.3%)	18 (60.0%)	46 (60.5%)
Types V/VI	5 (16.7%)	1 (6.3%)	3 (10.0%)	9 (11.8%)
BMI (kg/m²)				
Mean (SD)	24.8 (3.97)	27.5 (5.68)	24.6 (5.37)	25.3 (5.01)
Vitamin D (ng/mL)				
Mean (SD)	28.4 (11.23)	29.8 (9.48)	30.1 (12.43)	29.4 (11.28)
Total IgE (KIU/L)				
Median (IQR)	197.5 (61.7,536.0)	37.6 (20.1,117.5)	25.3 (12.6,55.3)	49.2 (21.0,180.5)
Parathyroid Hormone (pg/mL)				
Mean (SD)	36.1 (11.58)	31.6 (10.76)	35.0 (11.72)	34.7 (11.44)
Creatinine (mg/dL)				
Mean (SD)	0.8 (0.15)	0.8 (0.16)	0.8 (0.14)	0.8 (0.15)
Calcium (mg/dL)				
Mean (SD)	9.5 (0.33)	9.3 (0.32)	9.3 (0.35)	9.4 (0.35)

Table 2

Site × Season	Vitamin D			Placebo			Total (N=76)
	AD	Non-AD	Psoriasis	AD	Non-AD	Psoriasis	
San Diego (UCSD)	7 (9%)	7 (9%)	8 (11%)	8 (11%)	8 (11%)	8 (11%)	46 (61%)
Summer	4 (5%)	0	4 (5%)	3 (4%)	0	4 (5%)	15 (20%)
Fall	0	0	2 (3%)	3 (4%)	0	2 (3%)	7 (9%)
Winter	3 (4%)	7 (9%)	2 (3%)	2 (3%)	7 (9%)	2 (3%)	23 (30%)
Spring	0	0	0	0	1 (1%)	0	1 (1%)
Denver (NIJH)	4 (5%)	4 (5%)	0	4 (5%)	3 (4%)	0	15 (20%)
Summer	3 (4%)	2 (3%)	0	2 (3%)	0	0	7 (9%)
Fall	0	0	0	0	0	0	0
Winter	0	2 (3%)	0	1 (1%)	1 (1%)	0	4 (5%)
Spring	1 (1%)	0	0	1 (1%)	2 (3%)	0	4 (5%)
Oregon (OHSU)	4 (5%)	4 (5%)	0	3 (4%)	4 (5%)	0	15 (20%)
Summer	1 (1%)	0	0	0	0	0	1 (1%)
Fall	0	0	0	0	0	0	0
Winter	0	1 (1%)	0	0	0	0	1 (1%)
Spring	3 (4%)	3 (4%)	0	3 (4%)	4 (5%)	0	13 (17%)