

Correspondence

Reply

To the Editor:

We thank Thijs et al¹ for the helpful comments on our article.² Indeed, this correspondence led to the identification of misassignments of healthy controls and atopic eczema. We therefore re-performed our analysis, which led to the identification of significantly different serum levels for CCL17, CCL22, CXCL-10, IgE, and lactate dehydrogenase between healthy controls and patients with atopic eczema. CCL17 levels in the healthy control group are now lower, yet still range from 56 pg/mL to 979 pg/mL, with an average of 169 ± 202 pg/mL (mean $\pm$ SD) in our cohort. Despite high interindividual variations in the CCL17 expression levels in patients with atopic eczema (4629 ± 9559 pg/mL), we can confirm an overall correlation of CCL17 with the SCORing Atopic Dermatitis (SCORAD) (Pearson correlation coefficient of log10-transformed CCL17 is 0.450; adjusted P value = .00084; 95% CI, 0.201-0.643) in our data set. This correlation is in the lower range when compared with the cross-sectional studies of the meta-analysis by Thijs et al.³ This further hints at large disease variability, which is in line with the broad acceptance in the field and underpins the need of a multimarker biomarker to predict the severity of atopic eczema rather than a single biomarker. Similar to the multimarker disease severity model developed by Thijs et al,⁴ predictions of the SCORAD using our multimarker model are correlated with the original/clinical SCORAD values at 0.759 (95% CI, 0.612-0.855). However, computing the correlation coefficient between predicted and true values cannot assess the goodness of the fit of any predictive model. This is best demonstrated using our SCORAD model: despite the good overall correlation, the mean squared prediction error estimated by leave-one-out cross-validation pinpoints a prediction error of 18.9 SCORAD points at patient level. Thus, even this optimized best-fit prediction model underestimates or overestimates the severity of atopic eczema by 20%. We, therefore, cannot compare our findings to the model of Thijs et al, which was not evaluated by

any model-based quality measure. Overall, we agree with the conclusions of Thijs et al that the combination of biomarkers and usage of bioinformatics tools may be the way to develop more reliable and stable tools to monitor disease severity; however, arguing from our data, we still may lack the perfect markers to be included into these sophisticated models. Currently, there is an unmet medical need to predict disease severity of atopic eczema at individual patient's level.

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