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Analysis of *FcαRI* rs16986050 polymorphism in relation to autoimmune responses in dermatitis herpetiformis: an issue probing study

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Dear Editor,

Dermatitis herpetiformis (DH) is an autoimmune blistering dermatosis (ABD) associated with gluten intolerance [1, 2]. It is postulated that DH is a blistering skin manifestation of gluten-sensitive enteropathy (celiac disease). However, the precise molecular relationship is still not fully understand. The presence of various proteins (epidermal transglutaminase – eTG, tissue transglutaminase – tTG, nonapeptides of gliadin – npG) and the lack of precise identification of a specific individual molecule [3] suggests that DH is unlikely to be a classical autoantigen-driven autoimmune disease. Thus, specific genetic susceptibility, as well as environmental factors, is implicated in DH induction and progression. The involvement of the impaired human immunoglobulin A (IgA) Fc receptor (FcαRs) regulatory system is proposed, which may be linked to the activation of disease. The affinity of IgA Fc receptors (FcRs) to the autoimmune response in DH may vary based on single-nucleotide polymorphisms (SNPs) influencing the course and severity of the disease. Based on our previous studies [3, 4] FcαI/CD89 seems to be the most promising candidate associated with the immune response during DH development. FcαI/CD89 is a transmembrane glycoprotein binding both IgA1 and IgA2. CD89 shows abundant expression on human neutrophils and mediates inflammatory responses to IgA-immunocomplexes. The functional polymorphism 844 A>G in *FCAR/CD89* (rs16986050) is associated with a proinflammatory response, and with a higher percentage of cells with the formation of neutrophil extracellular trap (NET) [5]. However, there seem to be no data or consensus concerning *FCAR/CD89* polymorphisms in DH.

This study aimed to investigate the role of the *FCAR/CD89* SNP (rs16986050) missense polymorphism in the genetic predisposition to DH susceptibility concerning the autoimmune response.

In total, 48 subjects were investigated: 17 DH patients with an active skin rash before initiation of treatment and 31 healthy individuals (a local bioethical committee agreement, 541/13, Poland, 2013). The examined material consisted of perilesional skin tissues, sera, and EDTA-aspired whole blood. ELISA tests, direct immunofluorescence (DIF), TaqMan SNP Genotyping Assay, and statistical analysis were performed.

The greatest relative risk (odds ratio, OD) was reported for GG (rs16986050 of *CD89*) homozygotes (Table 1), albeit statistically insignificant ($p = 0.3306$). There was no statistically significant deviation from the Hardy-Weinberg equilibrium. There was no statistically significant relation between rs16986050 of *CD89* and IgA tissue-bound antibodies. There were no statistically significant differences between the genotypes of rs16986050 and specific anti-tTG IgA circulating autoantibodies.

The results of this issue-probing study suggest that the rs16986050 polymorphism, located in the coding region of *CD89*, is not associated with DH autoimmunity. Altogether, we could not demonstrate a role for the *CD89* 844A>G variant in the DH autoimmunity response, either as a locally dependent process or a systemic reaction. Nev-

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Table 1. Distribution of alleles and genotypes of rs16986050 in the examined DH population and healthy controls

rs16986050	DH (*n* = 17) *n* (%)	Controls (*n* = 31) *n* (%)	OR (95% CI)	*p* value
Allele				
A	23 (68)	46 (74)	0.73 (0.29-1.82)	0.3255
G	11 (32)	16 (26)	2.00 (0.85-4.70)	
Genotypes				
AA	9 (53)	17 (55)	0.92 (0.28-3.04)	1.000
AG	5 (29)	12 (39)	0.66 (0.18-2.35)	0.7531
GG	3 (18)	2 (6)	3.11 (0.46-20.77)	0.3306
pHW	0.1762	0.9517		

DH – dermatitis herpetiformis, n – number of patients, OR – odds ratio, CI – confidence interval, pHW – Hardy-Weinberg p-value

ertheless, it remains to be elucidated whether rs16986050 influences autoinflammation (direct neutrophil stimulation) rather than autoimmunity in DH.

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