The significance of Toll-like receptor (TLR) 2 and 9 gene polymorphisms in psoriasis

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The ethiopathogenesis of psoriasis is complex, multifactorial and still not well understood. Nowadays, the systemic, inflammatory and autoimmunological aspects of psoriasis are being emphasized [1].

Toll-like receptors (TLR) are characterized as pattern-recognition receptors, which are capable of potently activating various cell types. Toll-like receptors downstream signalling pathways lead to the production of a wide range of immune stimulatory cytokines and chemokines. Aberrant activation of TLR may result in an unrestricted inflammatory response, so the receptors may play a role in the development of inflammatory and autoimmune disorders [2].

TLR1, 2 and 5 are constitutively expressed on the normal keratinocytes [3]. TLR1 and TLR2 expression is further upregulated in psoriatic lesions [3, 4]. Seung *et al.* found a higher expression of TLR4 in guttate psoriasis compared to the plaque type and controls [5]. Moreover, TLR5 and TLR9 were upregulated by transforming growth factor α (TGF-α) in psoriatic keratinocytes [6]. In another study, Begon *et al.* showed the expression of tumor necrosis factor α (TNF-α) and interleukin (IL)-8 induced by the TLR2, 3 and 4 signalling pathway via nuclear factor κB (NF-κB) nuclear translocation in psoriatic keratinocytes [7].

In the light of these facts, TLR genes seem to be interesting gene candidates involved in psoriasis pathogenesis.

In this study we clarified the effect of Arg753Gln TLR2 and –1237 T/C TLR9 gene polymorphisms on the risk and the clinical manifestation of psoriasis.

The study group consisted of 175 unrelated patients with psoriasis vulgaris and 170 healthy, unrelated, age- and sex-matched volunteers. The mean Psoriasis Area Severity Index (PASI) was 16.9; PASI > 10 was observed in 90 patients. In the study group there were 121 (78.1%) patients with early onset (< 40 years) and 39 with late onset psoriasis (≥ 40 years). The gene polymorphisms were analyzed using the amplification refractory mutation system polymerase chain reaction method (ARMS-PCR).

There was no statistically significant association between genotype and allele frequencies in psoriatic patients in comparison with controls (Table 1). However, the presence of allele G in Arg753Gln TLR2 polymorphism was statistically more frequent in the group with late onset psoriasis in comparison with early onset psoriasis (100% vs. 96.2%; $p = 0.0127$). The presence of allele T in –1237 T/C TLR9 polymorphism was more common in the group of early onset psoriasis (86.3% vs. 73.8%; $p = 0.0086$) and their presence increases more than twice the risk of the development of this type of the disease

Table 1. Genotype and allele frequencies for Arg753Gln TLR2 and –1237 T/C TLR9 gene polymorphisms in control subjects ($n = 170$) and patients with psoriasis ($n = 175$)

Genotypes and alleles	Controls	Psoriasis	*P*-value
Arg753Gln TLR2	*N* = 170	*N* = 175	0.67
GG	162 (95.3%)	165 (94.3%)	0.67
GA	8 (4.7%)	10 (5.7%)	0.67
AA	0 (0.0%)	0 (0.0%)	
	N = 340	*N* = 350	
G	332 (97.6%)	340 (97.1%)	0.68
A	8 (2.4%)	10 (2.9%)	
–1237 T/C TLR9	*N* = 170	*N* = 175	0.39
TT	135 (79.4%)	128 (73.1%)	0.36
TC	26 (15.3%)	35 (20.0%)	0.47
CC	9 (5.3%)	12 (6.9%)	0.64
	N = 340	*N* = 350	
T	296 (87.1%)	291 (83.1%)	0.14
C	44 (12.9%)	59 (16.9%)	

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(OR = 2.23, p = 0.098). Moreover, TT –1237 T/C TLR9 genotype polymorphism was statistically more frequent in patients with PASI score > 10 (78.13% vs. 63.04%; p = 0.035). In the group of patients with PASI score > 15 TT genotype was also more frequent (79.66% vs. 68.67%; p = 0.38).

The true impact of the TLR polymorphisms on psoriasis susceptibility and course still remains unclear. In our research the study group was divided into early and late onset psoriasis due to epidemiological, genetic, immunopathological and clinical dissimilarities associated with these two types of the disease. Despite the fact that our results have not shown any association between TLR polymorphism and psoriasis susceptibility, we demonstrated the potential influence of these polymorphisms on clinical disease presentation. Romani *et al.* [8] found a relationship between TLR9 –1486 T/C SNP variants and a better response to narrow-band UVB phototherapy. Individuals bearing TC or CC genotypes showed a higher improvement of PASI score compared to patients with TT genotype. The TLR9 activation prompts an inflammatory pathway driven by interferon and IL-12 [8]. The blockade of TLR9 has been proposed also as a potential therapeutic target in psoriasis vulgaris [9].

In conclusion, the presented data do not prove the pathogenetic role of TRL2 and TLR9 polymorphisms in psoriasis development, however, they may have influence the clinical course of the disease. Further investigations are strongly required.

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Conflict of interest

The authors declare no conflict of interest.

References

1. Boehncke WH, Schön MP. Psoriasis. Lancet 2015; 386: 983-94.
2. Chen JQ, Szodoray P, Zeher M. Toll-like receptor pathways in autoimmune diseases. Clin Rev Allergy Immunol 2016; 50: 1-17.
3. Baker BS, Ovigne JM, Powles AV, et al. Normal keratinocytes express Toll-like receptors (TLRs) 1, 2 and 5: modulation of TLR expression in chronic plaque psoriasis. Br J Dermatol 2003; 148: 670-9.
4. Hari A, Flach TL, Shi Y, Mydlarski PR. Toll-like receptors: role in dermatological disease. Mediators Inflamm 2010; 2010: 437246.
5. Seung NR, Park EJ, Kim CW, et al. Comparison of expression of heat-shock protein 60, Toll-like receptors 2 and 4, and T-cell receptor gammadelta in plaque and guttate psoriasis. J Cutan Pathol 2007; 34: 903-11.
6. Miller LS, Sørensen OE, Liu PT, et al. TGF-alpha regulates TLR expression and function on epidermal keratinocytes. J Immunol 2005; 174: 6137-43.
7. Begon E, Michel L, Flageul B, et al. Expression, subcellular localization and cytokinic modulation of Toll-like receptors (TLRs) in normal human keratinocytes: TLR2 up-regulation in psoriatic skin. Eur J Dermatol 2007; 17: 497-506.
8. Romaní J, Julià M, Lozano F, et al. Toll-like receptor 9 promoter polymorphism as a predictive factor of narrow-band UVB phototherapy response in patients with psoriasis. Photodermatol Photoimmunol Photomed 2015; 31: 98-103.
9. Suárez-Fariñas M, Arbeit R, Jiang W, et al. Suppression of molecular inflammatory pathways by Toll-like receptor 7, 8, and 9 antagonists in a model of IL-23-induced skin inflammation. PLoS One 2013; 8: e84634.