Genetic Variability in Vascular Endothelial Growth Factor A and Risk of Psoriasis

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Psoriasis is a chronic autoimmune disease characterized by epidermal hyperplasia, dermal inflammation and neoangiogenesis. Vascular endothelial growth factor A (*VEGFA*), a key regulator of angiogenesis, is overexpressed in psoriatic skin. Although certain *VEGFA* gene polymorphisms have been associated with autoimmune conditions, their role in psoriasis remains unclear, particularly among Caucasian populations. To investigate the association of three *VEGFA* promoter polymorphisms –rs699947 (−2578 C/A), rs2010963 (+405 G/C) and rs1570360 (-1154 G/A)– with psoriasis susceptibility, age at onset and the Koebner phenomenon in a Southeastern European Caucasian population. A total of 194 psoriasis patients and 476 ethnicity-matched general population controls were genotyped using qPCR and melting curve analysis. Genotypic and allelic distributions were evaluated under five genetic models. Associations were assessed using odds ratios (ORs) with 95% confidence intervals (CIs). The *rs699947* C allele was significantly associated with increased risk of psoriasis (OR = 1.52, p = 0.001), particularly under the additive model. *rs2010963* and *rs1570360* polymorphisms showed no association with disease susceptibility. Within the psoriasis cohort, the *rs699947* C allele and CC genotype, as well as the *rs2010963* CC genotype were more frequent in patients with late-onset disease. However, the A allele and AA genotype of *rs1570360* were more prevalent among patients with early psoriasis onset. Additionally, the *rs2010963* C allele and GC genotype were underrepresented in patients exhibiting the Koebner phenomenon (OR=0.61, $p < 0.05$), suggesting a protective effect. These findings suggest a role for *rs699947* in susceptibility to and age at onset of psoriasis, and for *rs2010963* and *rs1570360* in age onset and modulating risk for trauma-induced lesion development. These *VEGFA* promoter gene variants may hold potential as molecular biomarkers for genetic risk stratification and personalized management in psoriasis.