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MC1R genotype and psoriasis: is there a link revealing a phenotypic difference? A pilot study

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Text

Editor

Psychological stress is known to trigger inflammatory skin diseases such as psoriasis. Recently, levels of hormones derived from pre-opiomelanocortin (POMC) were related with different types of psoriasis. [1] In particular, α –MSH, a POMC derivative, is known for its role in pigmentation and for its anti-inflammatory activity. Accordingly, it has been recently suggested for the treatment of imiquimod-induced psoriasis.[2,3]

For this reason, we decided to investigate the status of α-MSH receptor, the melanocortin 1 receptor (MC1R). The MC1R gene is a highly polymorphic gene codifying for a transmembrane G-protein coupled receptor. Some MC1R alleles have been associated with fair skin, increased sensitivity to ultraviolet (UV) radiation (the 'so called' RHC phenotype associated with RHC variants), psoralen–UVA photochemotherapy erythemal sensitivity, a worse outcome of melanoma patients treated with anti-BRAF and increased skin cancer risk.[4-9] Nevertheless, its role in skin inflammatory diseases, as compared to non-psoriatic controls, has not been previously described.

We report herein a preliminary analysis of MC1R genotype in psoriatic patients, as compared to non-psoriatic controls. Participants were recruited from a single Dermatology Unit (Bari). We included 24 consecutive patients affected by stable plaque psoriasis lasting at least 6 months (3 of which affected by psoriatic arthritis) and 53 controls.

Clinical skin examination, detailed questionnaire and MC1R sequencing, after signing a written informed consent, were performed for all subjects enrolled and reported in Table 1. MC1R genotype and sequence analysis were performed as previously described.[5] Table 2 shows MC1R genotype in both cases and controls. Procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration.

Statistical analysis was performed using SPSS statistical package (IBM, Armonk, NY, U.S.A.).
The univariate analysis highlighted a significant association between psoriasis and dark skin (p=0.007;OR 3,854, 95 % CI 1,399–10,617), hair (p=0,039), and eye color (p=0.026; OR 3,548, 95 % CI 1.064–11.835). Furthermore psoriasis is associated with absence of multiple MC1R variants (p=0,014) (Table 1).

We show that dark skin, hair and eye color are related to psoriasis while the presence of MC1R multiple variants is a protective factor in psoriatics, as compared to controls. MC1R polymorphisms are related to different degrees of receptor functional impairment, depending on the specific polymorphism and number of variants.[5,6]As a matter of fact, our results show that psoriatic patients are more likely to be wt or carriers of a single MC1R polymorphism. These data suggest that the preserved functionality of MC1R in psoriatics can

be related to peculiar phenotypic features (dark skin, eye and hair color), as compared to controls. Interestingly, the functional integrity of MC1R in psoriatic patients would be essential to exert the antinflammatory effects due to the binding of α-MSH and related analogues.[10] This is the first paper focusing on the role and the possible impact of MC1R genotype in psoriasis A limitation of our study is the number of patients enrolled. Further investigation are necessary to confirm these results.

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Table 1. Results of the univariate analysis

		Psoriasis (%)	Control (%)	p[+]
Sex	female	8 (33,3)	27 (50,9)	0,151*
	male	16 (66,7)	26 (49,1)	
Age	≤50	16 (66,7)	24 (45,3)	0,082*
	>50	8 (33,3)	29 (54,7)	
Smoking habits		8 (33,3)	14 (56)	0,534*
Alcohol addiction		4 (16,7)	14 (56)	0,4[#]
Hair color	light (red and blond)	0	10 (18,9)	0,026[#]
	Dark (brown and black)	24 (100)	43 (81,1)	
Eye color	light (blue or gray, green or hazel)	4 (16,7)	22 (41,5)	0,039[#]
	dark (light brown and dark brown)	20 (83,3)	31 (58,5)	
Skin color	light	9 (37,5)	37 (69,8)	0,007*
	dark	15 (62,5)	16 (30,2)	
Number of nevi	≤50	20 (83,3)	46 (86,8)	0,732[#]
	>50	4 (16,7)	7 (13,2)	
Multiple MC1R variants		0	11 (20,7)	0,014[#]

[+]A P-value < 0,05 was considered significant

*Pearson chi-square test

[#] Fisher's exact test

Table 2. MC1R genotype

MC1R status		**Psoriasis**	**%**	**Control**	**%**
wt or silent polymorphism		9	37,5	17	32
single polymorphism	*V60L*	10	41,7	10	19
	RHC variants	4	16,7	11	21
	others	1	4,1	4	8
multiple polymorphisms		0		11	21