GENETICS AND GENODERMATOSES

EVIDENCE OF COMMON AND DIFFERENTIAL GENETIC BIOMARKERS FOR PS AND PSA

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Introduction: Collagens provide stability and resilience to extracellular matrix of connective tissues, including dermis, blood vessels and bone. Collagen genes could be therefore involved in the etiopathogenesis of Psoriasis (Ps, OMIM#177900) and Psoriatic Arthritis (PsA, OMIM#607507), which are characterized by a dysfunction and instability of the connective tissues. COL10A1 (rs3812111, A/T), COL6A5 (rs12488457, A/C), COL8A1 (rs13081855, G/T) and the miR-146a (rs2910164, G/C) were selected as potential biomarkers for Ps and PsA susceptibility.

Materials and Methods: 1417 Italian subjects (393 Ps, 424 PsA and 600 controls) were genotyped by Real Time-PCR for rs12488457 (A/C, COL6A5), rs13081855 (G/T, COL8A1), COL10A1 (rs3812111, A/T) and rs2910164 (G/C, miR-146a). and subjected to biostatistical analysis using chi-square test and evaluation of ORs. The potential pathogenetic impact of the associated genes was then investigated by bioinformatic tools.

Results: the rs12488457 (A/C, COL6A5), rs13081855 (G/T, COL8A1) and rs2910164 (G/C, miR-146a) resulted to be associated with both Ps [rs12488457: p=2.97*10-9;, OR (C): 1.75, CI95%: 1.44-2.13; rs13081855: p=0.001, OR (T): 1.79, CI95%:1.24-2.59; rs2910164: p=0.01, OR (G): 1.29, CI95%:1.04-1.61] and PsA [rs12488457: p=1.24*10-5, OR (C): 2.46, CI95%: 2.03-2.97; rs13081855: p=9.06*10-6, OR (T): 2.17, CI95%:1.53-3.06; rs2910164: p=0.04, OR(G): 1.23 CI95%:1.0-1.51]. The rs3812111 (A/T, COL10A1), instead, showed significant association with PsA only [p=0.008, OR (T):1.29, CI95%:1.07-1.57]. The bioinformatic analysis reported that COL6A5, COL8A1 and miR-146a are likely to be involved in proliferation, neovascularization and inflammation

pathways which are known to be disrupted in Ps and PsA. On the other hand, COL10A1 was implicated in bone metabolism which is strongly dysregulated in PsA patients.

Conclusions: these data allowed the identification of COL6A5, COL8A1, miR-146a and COL10A1 as novel susceptibility biomarkers for Ps and PsA, highlighting thereby the existence of different etiopathogenetic mechanisms for these pathologies.