PSORIASIS

IFN-G, TNF-A AND IL-17 PRO-INFLAMMATORY CYTOKINES REGULATE THE EXPRESSION OF GENES INVOLVED IN MIRNA BIOGENESIS IN NORMAL AND PSORIATIC KERATINOCYTES

C Tuccilli [1] - S Madonna [2] - E Baldini [1] - C Scarponi [2] - F Persechino [3] - D Giordano [3] - S Persechino [3] - C Albanesi [2] - S Ulisse [1]

"sapienza" University Of Rome, Department Of Surgical Sciences, Rome, Italy [1] - Istituto Dermopatico Dell'immacolata Idi-irccs, Laboratory Of Experimental Immunology, Rome, Italy [2] - "sapienza" University Of Rome, Nesmos Department, Rome, Italy [3]

Background: Psoriasis is a chronic, immune-mediated inflammatory skin disease characterized by an abnormal gene expression, influenced by both genetic and environmental factors. In particular, about 250 microRNAs (miRNAs) have been found deregulated in psoriatic lesions, and are thought to contribute to the pathogenesis.

Objective: To evaluate whether the mRNA levels of key genes involved in miRNA biogenesis, namely DROSHA, DICER, DGCR8, EXP5 and AGO2, are affected by IFN-γ, TNF-α and IL-17, three inflammatory cytokines aberrantly present in psoriatic lesions and targeting keratinocytes.

Materials and Methods: Primary keratinocytes cultures were established from skin biopsies of 4 healthy volunteers or 4 psoriatic patients. Second- or third-passage keratinocytes were grown for at least 3-5 days and 18-h stimulated with IFN-γ (200 U/ml) plus TNF-α (50 ng/ml) and IL-17 (50 ng/ml) or left untreated. Then, mRNAs of the above-mentioned genes and ribosomal RNA 18S were evaluated by quantitative RT-PCR.

Results: In basal conditions, no significant differences in gene expression were observed between normal and psoriatic keratinocytes. Following cytokine treatment, the expression of DROSHA and EXP5 was significantly decreased ($p<0.05$) in both normal and psoriatic keratinocytes by about 35-45%, and a similar trend was observed for DGCR8. Conversely, the expression of AGO2 was increased by about 35% ($p<0.05$) in normal, but not in psoriatic, keratinocytes, while DICER expression was unaffected by cytokine treatment.

Conclusion: We showed no differences in the expression levels of genes involved in miRNA biogenesis between normal and psoriatic keratinocytes. However, IFN-γ plus TNF-α and IL-17 affected the expression levels of DROSHA, DGCR8, EXP5 and AGO2 in both normal and psoriatic keratinocytes. Our observations support the hypothesis that the inflammatory

environment, other than genetic factors, could contribute to the observed alterations in miRNA expression profile, through deregulation of the expression of genes involved in miRNA biogenesis.