

## Genetic Predisposition to Cutaneous Sarcoidosis

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Sarcoidosis is a systemic noncaseating granulomatous disease that can affect any organ, while lungs, lymph nodes, and skin seem to be the most commonly affected organs (1,2).

We read with interest the recent paper, entitled "Unusual manifestation of cutaneous sarcoidosis: a case report of morpheaform sarcoidosis", published in the *Acta Medica Iranica* (3). The authors presented a case of cutaneous sarcoidosis who suffered from multiple indurated scaly plaques resemble morphea with granulomatous pattern. The authors presented well the clinical phenotypes associated with sarcoidosis, but failed to discuss on pathophysiology of disease. Although the exact cause of sarcoidosis is unknown, causative role of environmental exposures in association with dysregulation in immunological processes have been suggested in formation and development of the disease (2,4). Despite the significant role of environmental factors (such as microbial agents and infections) (5-7), the importance of genetic factors in susceptibility to the disease should not be disregarded (8).

Genetic analysis revealed some predisposing genes related to sarcoidosis. The majority of investigations were performed on the human leukocyte antigen (HLA) system genes, especially DRB1 and DQB1 (9), while some other genes including *BTNL2*, *CCR2* and *ACE*, which are generally involved in antigen presentation, cytokine responses, and cell signalling, have also been suggested (10,11). A study on in skin biopsies of patients with cutaneous sarcoidosis showed increased *Gli-1* oncogene expression, which is a transcription factor mediating the hedgehog signalling pathway (12). Although some other candidate genes, including *SERPINB1*, *FABP4*, *S100A8*, *HBEGF*, *IL7R*, *LRIG1*, *PTPN23*, *DPM2* and *NUP214* have been investigated in different studies (13), genome-wide association studies (GWAS) confirmed the association of HLA and *BTNL2* with sarcoidosis, while two new genes, including *ANXA11* and *RAB23*, were also suggested. *ANXA11* seems affect the apoptosis pathway, while *RAB23* seems

to be involved in antibacterial defense processes (11,14,15).

Considering the complex interaction between environmental and genetic risk factors, preparing a molecular profile for patients with cutaneous sarcoidosis would be an efficient technique in development of diagnostic protocols. Furthermore, identification of predisposing genetic elements could be used to develop prognostic tools.

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