

**Hidradenitis suppurativa patients (HS, inverse acne)** is a chronic, progressive autoimmune, inflammatory skin disease affecting mainly the skin apocrine glands. HS is demonstrated by the appearance of painful abscesses distributed in apocrine-glands rich areas. The disease begins mostly in early adulthood. Notably, accumulating data confirm that HS is no longer considered as a disease caused by bacterial infection but is triggered by dysregulation of the innate immune system. Although the pathogenesis of HS remains unclear, various molecules is suggested to be involved i.e.: tumor necrosis factor alpha (TNF- $\alpha$ ), interferon gamma (IFN)- $\gamma$ , interleukin (IL)-1 $\beta$ , IL-6, IL-12, IL-17, IL-18 or IL-23 in combination with individual genetic predisposition and potentially an imbalance of the skin microbiome.

Growing prevalence of HS causes not only diagnostic but also disease management (further advancement risk, treatment) difficulties. In the light of growing interest in HS, significant efforts should be made to discover next-generation biomarkers for early diagnosis, prognosis and treatment monitoring of the disease.

Up to date there is no available specific biomarkers that would help in early diagnosis of patients with HS and distinguish symptoms from other inflammatory disorders (i.e.: bacterial abscesses). Moreover, there are no blood-based biomarkers which could estimate the prognosis and evaluate the efficacy of available therapies.

MicroRNAs (miRNAs, miRs) are a class of non-coding RNAs (ncRNAs). Due to their biochemical stability and abundance in different body fluids, for more than decade miRNAs emerged as potential novel biomarkers. MiRNAs are able to modulate various cellular functions through regulating gene expression, transcriptions and translation processes. Therefore miRNAs exert their functions as part of an epigenetic regulation network. To date few studies suggested that miRNAs are involved in regulating pathogenicity related gene expression of HS.

A key goal of HS management (early diagnosis, prognosis and treatment) is to avoid HS-caused suffering and disability, and to recover patients' quality of life. Therefore searching for novel molecular biomarkers associated with signaling pathways involved in pathogenesis of HS seems crucial. Discovering particular levels (increased or decreased) of circulating miRNAs strongly correlated with HS development and advancement would be highly helpful to diagnose early or even preclinical stages of HS. Additionally, particular miRNAs may serve as a tool to compare the efficacy of conventional treatment (antibiotics) and novel treatment (TNF $\alpha$  inhibitors).

Combining the knowledge about signaling pathways and underlying molecular mechanisms triggered by miRNAs, miRNAs-genes and genes-genes networks could be the next, crucial step in better understanding pathogenetic processes involved in HS development. A better understanding of the association of the expression of specific miRNAs molecules with pathophysiological processes observed in HS may confirm the utility of miRNAs as novel diagnostic/prognostic biomarkers in patients with this rare condition.

Evaluation of the effect of a particular treatment regimen on the expression levels of specific miRNAs will allow for comparison of the efficacy of different drug regimens, better treatment monitoring, as well as estimation of individual risk of HS exacerbation.

Our study will be the first study to analyze the expression of miRNAs and genes in the context of early diagnosis, disease progression, treatment monitoring and comparing the effectiveness of selected HS treatment regimens. Currently, no study is registered on clinicaltrials.gov to evaluate the utility of miRNAs as HS biomarkers. Our project can highly contribute to better understanding of the pathophysiology of HS and thus patients' outcomes.

Therefore, our study provide for the first time knowledge on the utility of miRNAs as diagnostic/prognostic biomarkers in a very unique population of HS patients before and twice during the treatments.