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**Background:** Moderate to Severe Plaque Psoriasis is an inflammatory skin disease that is associated with multiple comorbidities and substantially diminishes patients’ quality of life. As one of the most significant therapeutic advancements in the field of dermatology, Biologics such as TNF inhibitors, IL-12/23 inhibitor, IL-17 inhibitors, and IL-23 inhibitors, have higher efficacy compared with oral medications or phototherapy. However, the previous studies did not focus on the simultaneous comparison of molecular changes in different classes of biologics. The identification of time-series genes (TSGs) could help to uncover the mechanisms underlying transcriptional regulation.

**Objectives:** In this study, we aimed to compare the differences in expression patterns and functions of time-series genes in Moderate to Severe Plaque Psoriasis under different biologics treatments.

**Methods:** The transcription profile of GSE117239 and GSE51440 were obtained from the Gene Expression Omnibus database (GEO). The GSE117239 included 19 samples treated with Etanercept (TNF inhibitors) and 16 samples treated with Ustekinumab (IL-23 inhibitors). Skin biopsy samples (LS: lesion; NL: non-lesion) were collected at baseline, weeks 1 and 12, respectively. After background adjustment and other pre-processing, differentially expressed genes (DEGs) were extracted from LS skin biopsy and untreated NL skin biopsy at different times after three different biologics treatments, respectively. The Short Time-series Expression Miner (STEM) software was used to cluster and compare average DEGs with coherent changes. Afterward, the different expression patterns of TSGs under the three treatment groups were compared. GO analysis and KEGG pathway enrichment analysis of TSGs were performed by Metascape.

**Results:** Different DEGs varied in LS skin compared with those of NL skin biopsy: 978 genes in Ustekinumab group, 996 genes in Etanercept group, and 601 genes in Guselkumab group detailly (P < 0.05 and |log FC| > 1). Gene landscapes suggested the signatures of LS gradually changed during treatment process, and gradually converge to NL signatures (Fig 1a, 2a, 3a). Time-series genes in the three treatment groups had different expression patterns and functions. In the Ustekinumab group, a total of 448 TSGs in profile 3 showed a stable-stable-decreasing expression trend and significantly different from the other two groups.
associated with mitotic nuclear division and defense response to other organism, whereas in profile 4 represented a stable-stable-increasing expression trend and significantly associated with positive regulation of cellular response to organic 9 compound (Fig. 1). With the treatment of Etanercept, 22 TSGs had a stable-increasing-increasing expression tendency and closely associated with fatty acid metabolism and steroid metabolic process (Fig. 2). After Guselkumab treatment, 13 TSGs also represented a stable-increasing expression tendency that mainly characterized by defense response to other organism and epidermis development (Fig. 3). Interestingly, both Ustekinumab and Guselkumab treatment dramatically influenced defense response to other organism-related genes, while Etanercept mainly affected genes involved in fatty acid metabolism and steroid metabolic process.

Conclusion: Biologics effectively reconstituted the gene signatures of psoriasis in different aspects. TSG features could be one of indicator for precise intervention for psoriasis.

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