NOVEL FACTORSIN PSORIASIS PATHOGENESISANDPOTENTIAL DRUG CANDIDATESAREFOUNDWITH SYSTEMSBIOLOGYAPPROACH

Manczinger Máté[1], Kemény Lajos[1,2]

[1]Department of Dermatology and Allergology, University of Szeged, Hungary

[2]Dermatological ResearchGroup of the Hungarian Academy of Sciences, Szeged, Hungary

Introduction: Psoriasis is a multifactorial inflammatory skin disease characterized by increased proliferation of keratinocytes, activation of immune cells and susceptibility to metabolic syndrome. Systems biology approach makes it possible to reveal novel important factors in the pathogenesis of the disease.

Methods: Protein-protein, protein-DNA, merged (containing both protein-protein and protein-DNA) interactions and chemical-protein interaction networks were constructed consisting of differentially expressed genes (DEG) between lesional and non-lesional skin samples of psoriatic patientsand/or the encoded proteins. DEGs were determined by microarray meta-analysis using MetaOMICS package. We used STRING for protein-protein, CisRED for protein-DNA and STITCH for chemical-protein interaction network construction. General network-, cluster- and motif-analysis were carried out in each network.

Results and discussion: Many proteins (BUB1B, CCNA2, FYN and PIK3R1, SGK1) and transcription factors (AR, TFDP1) were identified as hubs, suggesting that these factors might be important in psoriasis pathogenesis. BUB1B, CCNA2 and TFDP1 might play a role in the hyperproliferation of keratinocytes, whereas FYN and SGK1 may be involved in the disturbed immunity in psoriasis. AR can be an important link between inflammation and insulin resistance in psoriasis. A controller sub-network was constructed from interlinked positive feedback loops that with the capability to maintain psoriatic lesional phenotype. Analysis of chemical-protein interaction networks detected 37 drugs with previously confirmed antipsoriatic effects, 29 drugs with some experimental evidences, and 25 drugs with case reports suggesting their disease modifying effects. In addition, 108 unpublished drug candidates were also found, that might serve future treatments for psoriasis.