CEBPB: a novel hub gene in skin inflammation and multifunctional disease driver in Psoriasis

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Abstract
Transcription factors represent key nodes that integrate signaling pathways to drive a plethora of downstream cellular responses. Using a novel approach, we identified CEBPB as a novel factor associated with skin inflammation. In spatial transcriptomics, bulk RNA Seq and IHC analysis, CEBPB was significantly upregulated in the lesional skin of Lichen planus (LP), atopic dermatitis (AD) and Psoriasis (Pso) patients with the strongest levels in Pso. Similarly, in vitro stimulated primary human keratinocytes showed the strongest CEBPB induction under Psorelevant cytokines. We show that loss of CEBPB completely inhibited the development of acanthosis, diminished the number of K67+ proliferating keratinocytes, reduced mitochondrial density and ATP levels indicating a downregulated metabolism. Moreover, CEBPB KO reduced secretion of neutrophil attracting chemokines. In line, CEBPB levels positively correlated with clinical scores of acanthosis and neutrophil infiltration. In summary, we demonstrate that CEBPB is associated with various pathogenic hallmarks of inflammatory skin diseases. Our findings hold substantial promise for the use of CEBPB as a new therapeutic target in skin inflammation.

Background
Identification of CEBPB via a computational approach linking gene expression to clinical phenotypes
- new insights into mechanisms of disease pathology
- validate as a novel biomarker and disease driver

CEBPB is upregulated in patients with CISDs with highest levels in Psoriasis

CEBPB regulation in vitro in primary keratinocytes

CEBPB controls the metabolic fitness of keratinocytes

CEBPB role in keratinocytes proliferation, acanthosis and neutrophil migration

3D disease model

Conclusion and Outlook

In conclusion, CEBPB:
- is upregulated in inflammatory skin conditions, highest in Psoriasis
- induces inflammatory cytokines and chemokines
- mediates keratinocytes proliferation, acanthosis and neutrophil migration
- serves as a therapeutic target in Psoriasis
- is a control point for pathogenic epidermal responses

CEBPB is a novel master transcription factor in keratinocytes, a key regulator of psoriasis disease pathology and a promising therapeutic target.