# The transcription factor Bcl11b: a new regulator of canonical and non-canonical NF-kB pathways

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## INTRODUCTION

Bcl11b, a zinc finger bi-functional transcription factor, is highly expressed in various tissues during development and differentiation such as skin and immune system. The canonical and non-canonical NF-kB pathways are known in immune-mediated inflammatory diseases, that can be activated by cytokine stimulation. However, the mechanism of cytokine activation and regulation of Bcl11b in relation to the NF-kB pathways is not completely understood.

## OBJECTIVES

To investigate the role of *Bcl11b* in the regulation of *NF-kB* pathways in keratinocytes as an example of psoriasis.

## METHODS & RESULTS

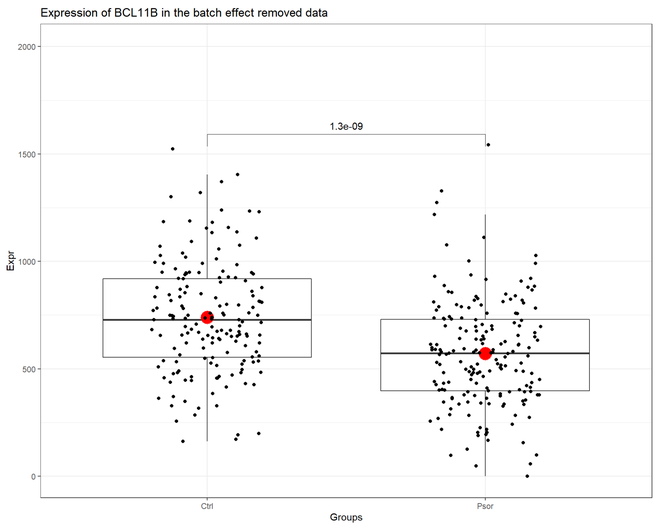
### Bioinformatics

Data base selection

GSE121212, GSE114286, GSE83645, GSE66511, GSE54456, GSE117405, GSE142582 and GSE107871

Data analysis (normalization & batch effect removal)

Identification of the expression level of Bcl11b

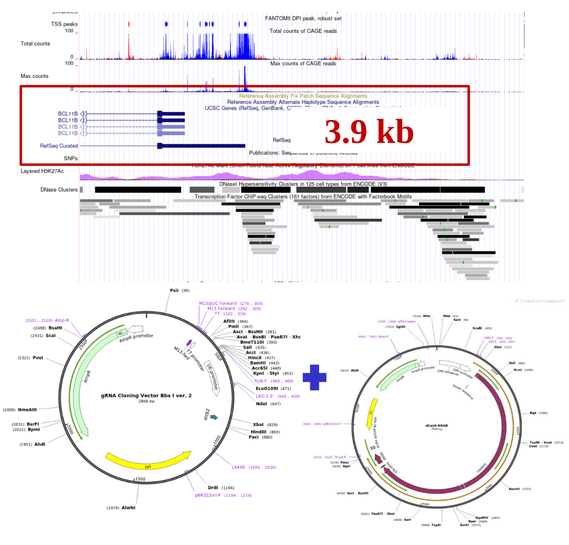



**Parsa.S.,et al (unpublished).**

- RNA-sequencing data sets of expression profiles by high throughput sequencing of lesional skin biopsies of psoriasis patients versus healthy skin controls obtained from the GEO database. All data were merged and batches were corrected.

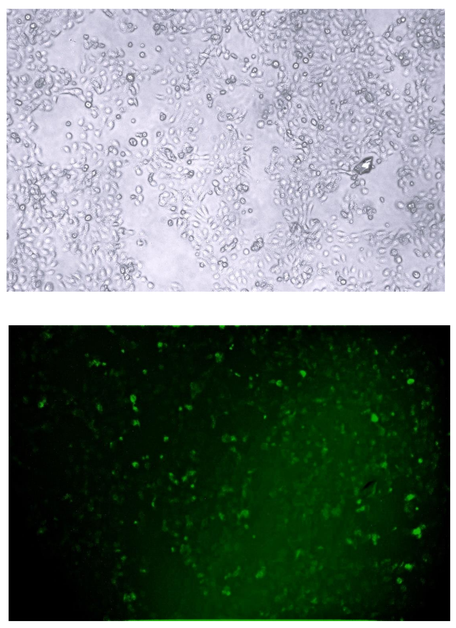
## METHODS & RESULTS

### Knock-down Bcl11b: gRNA designing & cloning



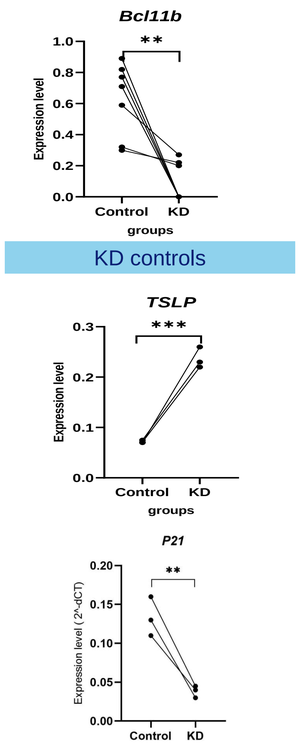

- **Promoter of *Bcl11b* was identified**
- **gRNAs were designed for the promoter region of *Bcl11b* .**
- **gRNAs were cloned in the carrier vector.**

### HaCaT cell Transfection

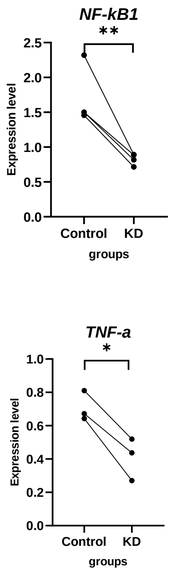


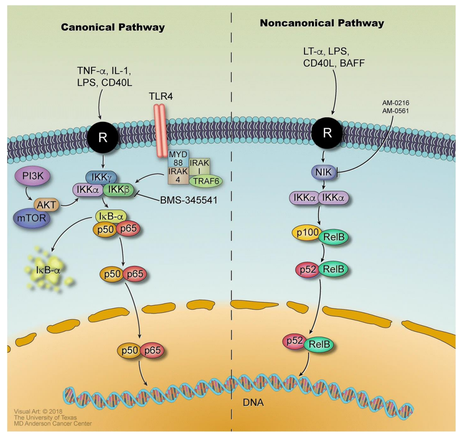
- **HaCaT cells were transfected with gRNA carrier vectors and d-Cas9-KRAB vector. GFP was used as a reporter gene.**

### qPCR results




### NF-kB canonical and non-canonical pathway

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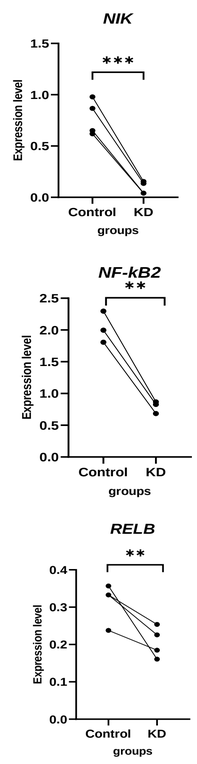
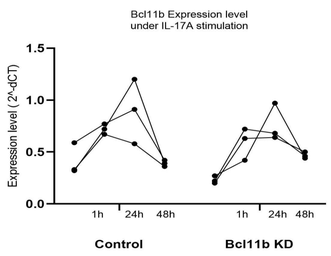


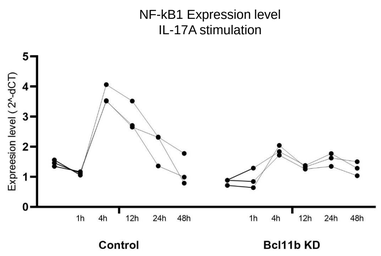

- **Expression level of different genes in canonical and non-canonical NF-kB pathways were measured in Normal and *Bcl11b* KD HaCaT cells**

### IL-17A, IL-23 and IL17A/IL-23 effect on Normal and KD HaCaT cells

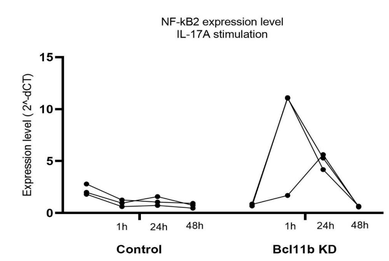
BCl11b expression level




NF-kB canonical Pathway




NF-kB non-canonical Pathway




## CONCLUSION

Here, for the first time, we showed the role of *Bcl11b* in psoriasis and its interaction with the canonical and non-canonical NF-kB pathways. Since *Bcl11b*, *NF-kB1* and *NF-kB2* are transcription factors, this study suggests that there is a mutual interaction between them. Furthermore, the data indicates the early activation of *NF-kB2* under IL-17A stimulation which can represent the effect of *NF*-kB2 on *Bcl11b* as well. Interestingly this effect is not shown using IL-23. Future study will include the mutual interaction of *Bcl11b*, *NF-kB1* and *NF-kB2*.

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