PRINS long non-coding RNA regulates psoriasis-associated immune responses of human keratinocytes

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BACKGROUND

We have previously demonstrated that PRINS IncRNA is differentially expressed in psoriatic uninvolved epidermis compared to either healthy or involved epidermis [1]. PRINS expression is altered by several cellular stressors and might be implicated in the stress response of keratinocytes [2]. A recently identified stressor and pathogenic factor in psoriatic epidermis are cytosolic DNA fragments, which induce inflammasome activation and inflammatory cytokine production [3]. Our aim was to analyse whether PRINS has any role in cytosolic DNA induction.

RESULTS

I. IL-6 and CCL-5 expression of NHEKs is regulated by PRINS

Expression and secretion of IL-6, CCL-5 and IL-8 was significantly decreased by PRINS overexpression, whereas mRNA expression and secretion of IL-1α, IL-1β and TNF-α were not affected. *p<0.05, **p<0.01

II. In silico analysis predicted a putative binding site between PRINS IncRNA and the mRNAs of IL-6 and CCL-5

PRINS-ΔPRINS

PRINS

CCL-5

IL-6

223 312 622

It has been recently reported that PRINS directly interacts with CCL-5 mRNA [5]. In an in silico analysis we have found an appr. 100 nt-long possible interaction site between the non-coding RNA of PRINS and the mRNA of IL-6 in a distance of appr. 200 nucleotides from the predicted CCL-5 binding site.

CONCLUSIONS

PRINS IncRNA directly binds to the IL-6 mRNA a cytokine implicated in the pathogenesis of psoriasis.

PRINS inhibits inflammatory reactions by decreasing IL-6 and CCL-5 levels.

We hypothesize that elevated level of PRINS in psoriatic uninvolved epidermis contributes to the normal phenotype by inhibiting inflammatory reactions of keratinocytes.

MATERIALS AND METHODS

• Normal human epidermal keratinocytes (NHEKs) were primed with TNF-α and IFN-γ and transfected with the synthetic DNA analogue poly(dA:dT).
• Expression of cytokines was measured by real-time RT-PCR and ELISA.
• PRINS construct was created by cloning the AK022045 cDNA sequence into a pcDNA3.1(+) vector. AΔPRINS construct was created by replacing the position 538–622 in the AK022045 cDNA sequence with a scrambled sequence and cloned into pcDNA3.1(+) vector. These constructs were used for vector overexpression and in vitro transcription.
• INTARNA was used for in silico prediction [4].
• In vitro binding assay was carried out using an MST instrument with the in vitro transcribed, full length PRINS and ΔPRINS RNA and fluorescently labelled, truncated IL-6 mRNA.

REFERENCES