USP2 as a potential link between miR-125b and psoriasis - DTU Orbit (02/12/2018)

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Background
The extensive involvement of microRNA (miRNA) in the pathophysiology of psoriasis is well documented. However, in order for this information to be useful in therapeutic manipulation of miRNA levels, it is essential that detailed functional mechanisms are elucidated. miR-125b has previously been shown to be strongly associated with psoriasis, and presents as an obvious candidate for further investigation.

Objectives
To elucidate the specific pathway and mechanism of interest in this association.

Methods
A three-step bioinformatical hypothesis-generation pipeline was performed to identify genes of interest. This pipeline was based on miR-125b binding, expression in psoriatic lesions and genome-wide association study-based evidence of involvement. The identified candidate gene was then carefully evaluated using luciferase binding assays, in vitro overexpression, small interfering RNA knock-down and downstream gene readouts.

Results
Based on our bioinformatical pipeline, ubiquitin-specific peptidase 2 was selected as a likely candidate for a mechanistic explanation for psoriasis association. After establishing a definite connection to miR-125b, we proceeded to show that modulation of nuclear factor kappa B-mediated inflammation is the likely mechanism through which this miRNA gene pair functioned.

Conclusions
Shedding further light on the multifactorial causes of psoriasis is essential, if the goal is to progress towards finer control of therapeutic tools in disease management. Findings, such as the ones presented herein, are therefore necessary in order to achieve the future of personalized medicine.

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