Targeting $miR-21$ to Treat Psoriasis

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• 22nt long non-coding RNAs
• Control expression and activity of protein coding genes
• Target silencing: mRNA decay or translation

miR-21

One of the most published miRNAs (Pubmed 2181 5.11.2015)
Known as an oncomiR
Screenings revealed a sig. upregulation of miR-21 in different solid tumor types and cancerous cell lines (Voglina et al., 2000)
miR-21 is implicated in aging (Dellago et al., 2013)
Human Skin

psoriasis

chronic inflammatory skin disease characterized by thickened, scaly skin lesions

- Defective interplay between KCs and inflammatory cells
- Increased prol. and impaired diff. of KCs
- Rete ridges
- Inflammatory cells infiltrate the dermal/epidermal boundaries
- Cause remains unknown
  - Environmental factors
  - Genetic predisposition for the gene-loci of S100A8 and JunB

Lowes et al., 2014
Expression of miR-181b, miR-221, miR-222 and miR-21 was analysed in the epidermis.
Epidermal laser capture microdissection

A

B

miR-21 ISH quantification

D

miR-21

E

TIMP-3

F

TNFα

Relative to SS: RNA

Relative to GAPDH mRNA

Relative to GAPDH mRNA

Non-lesional

Lesional
Double knockout mice with inducible epidermal deletion of JunB/c-Jun.

The mice mimic human disease in:
- hyper- and parakeratosis
- leukocyte infiltration
- intraepidermal T cells
- increased angiogenesis
- epidermal microabscesses

Zenz et al., 2005
To analyze whether miR-21 has a causal role in poriasis progression they used anti-miR-21.
To demonstrate that TIMP-3 are targets of miR-21 in psoriasis, they performed in vivo TIMP-3 restoration.
To demonstrate that TACE is a target of miR-21 in psoriasis, they performed in vivo TACE shRNA mediated knockdown.
Does miR-21 inhibition have a therapeutic benefit?
Does miR-21 inhibition alter barrier function?
Summary

miR-21

JunB/c-Jun

TIMP-3

TACE

mTNFα

sTNFα

TNFR1

TNF-dependent cytokines

Skin inflammation and cachexia

Psoriasis-like disease in adults

Perinatal death of newborns

IL-6

Jak/Stat