

# Targeting *miR-21* to Treat Psoriasis

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# microRNAs

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

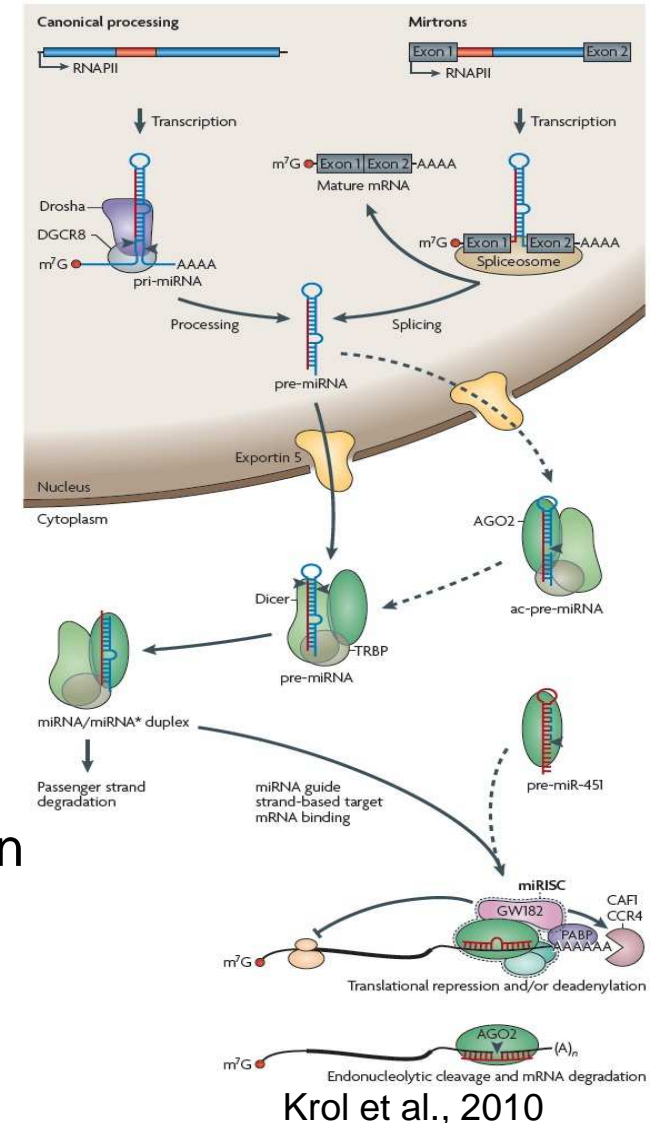
## miR-21

One of the most published miRNAs (Pubmed **2181** 5.11.2015)

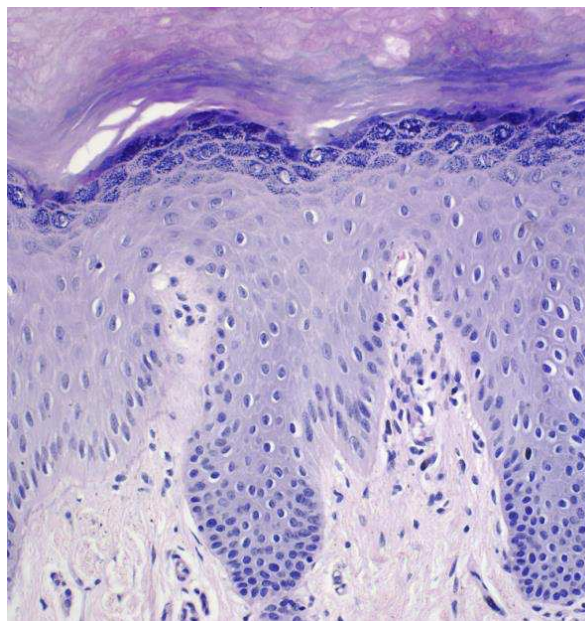
Known as an oncomiR

Screenings revealed a sig. upregulation of miR-21 in different solid tumor types and cancerous cell lines (Vogliana et al., 2000)

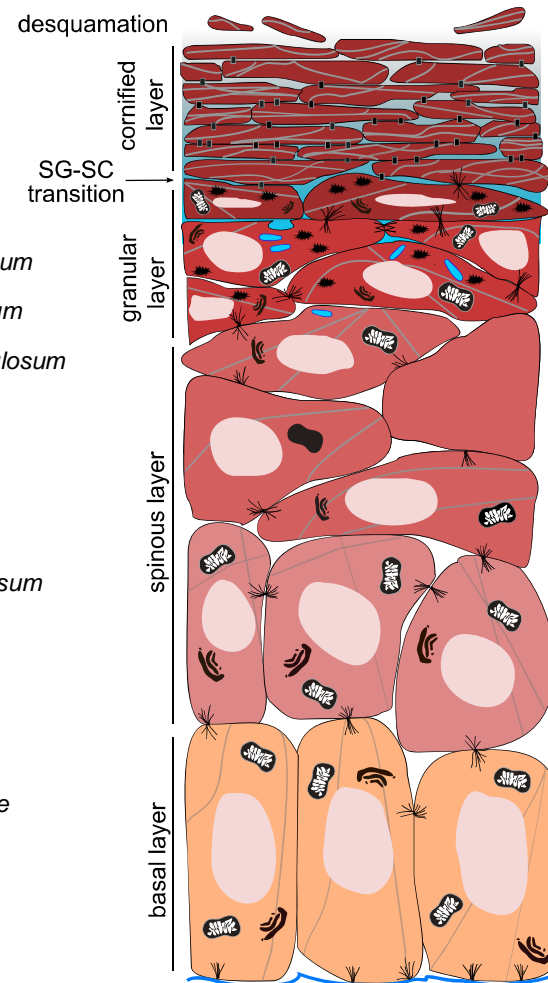
miR-21 is implicated in aging (Dellago et al., 2013)



# Human Skin



Stratum corneum  
Stratum lucidum  
Stratum granulosum  
Stratum spinosum  
Stratum basale



corneocyte shedding

filaggrin degradation  
desintegration of organelles  
LB extrusion: lipids and desquamating enzymes  
keratin filament strenghtening  
protein/lipid cross-linking by transglutamination  
caspase-14 activation  
EDC expression

K1, K10, caspase-14  
expression

proliferation

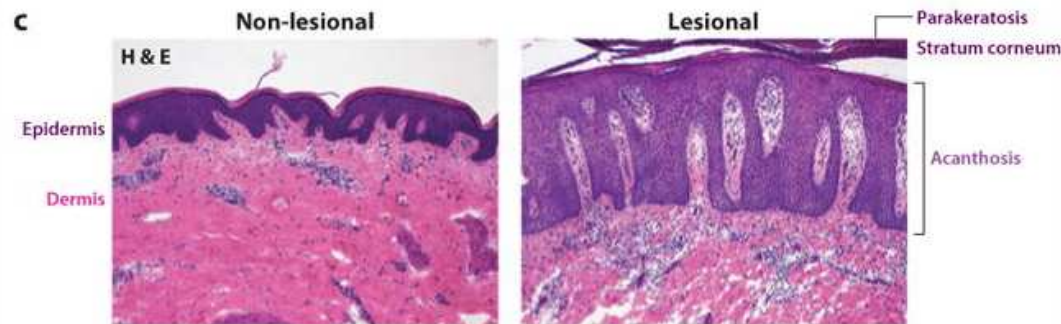
K5, K14 expression

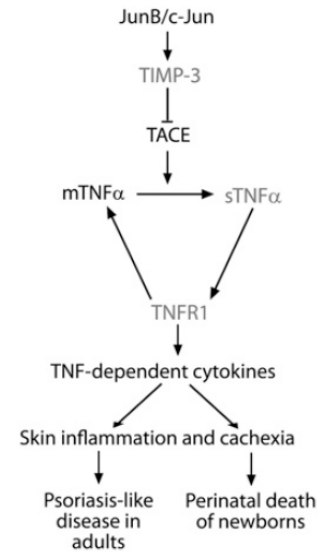
# Psoriasis

chronic inflammatory skin disease characterized by thickened, scaly skin lesions



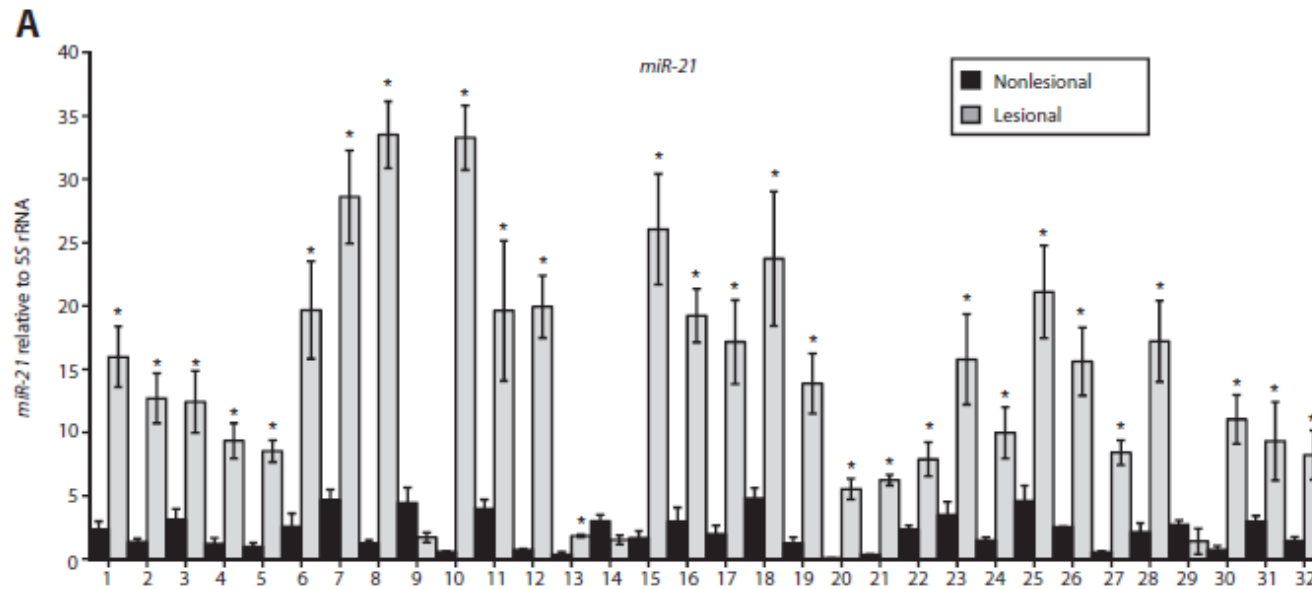
- Defective interplay between KCs and inflammatory cells
- Increased prol. and impaired diff. of KCs
- Rete ridges
- Inflammatory cells infiltrate the dermal/epidermal boundaries
- Cause remains unknown
  - Environmental factors
  - Genetic predisposition for the gene-loci of S100A8 and JunB

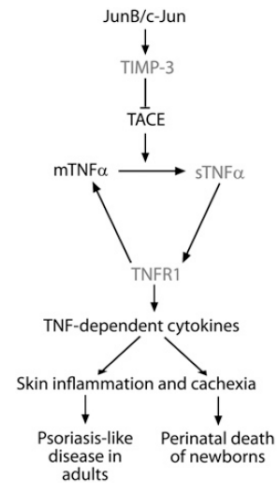




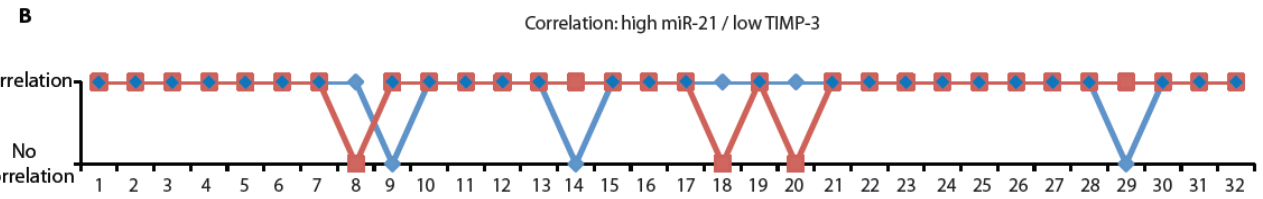
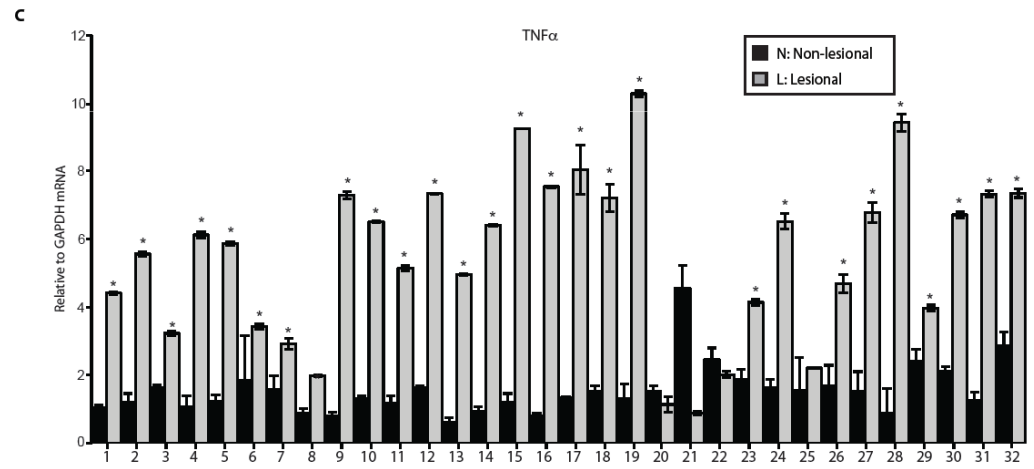
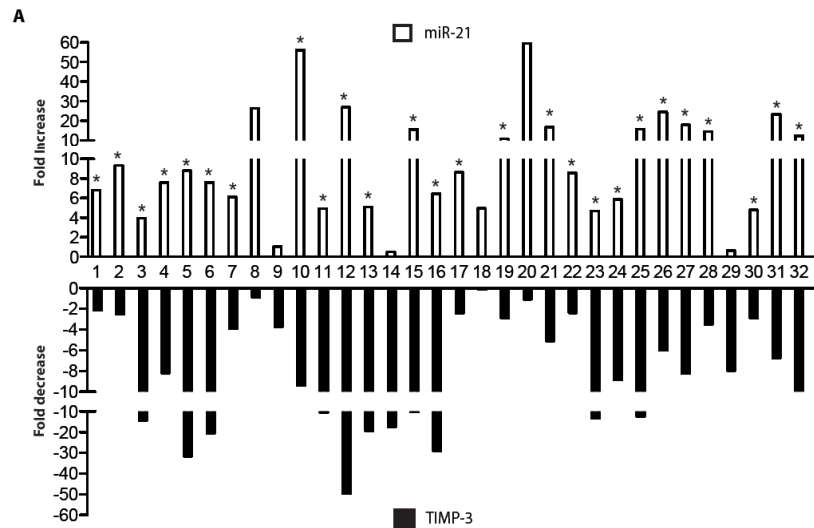
Guinea-Viniegra et al., 2009

Expression of miR-181b, miR-221, miR-222 and miR-21 was analysed in the epidermis



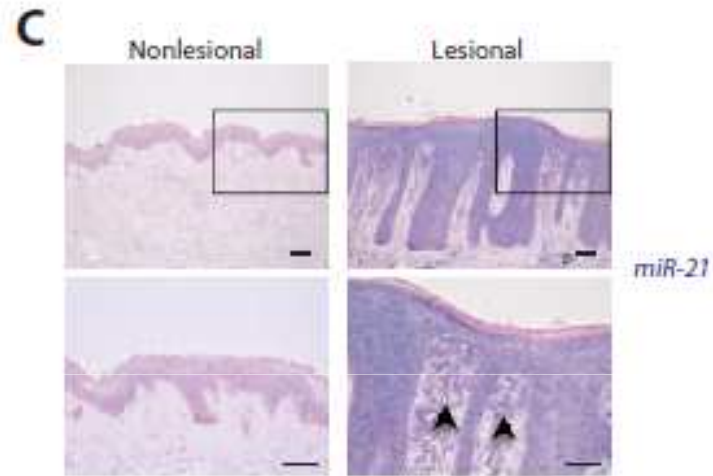


Guinea-Viniegra et al., 2009

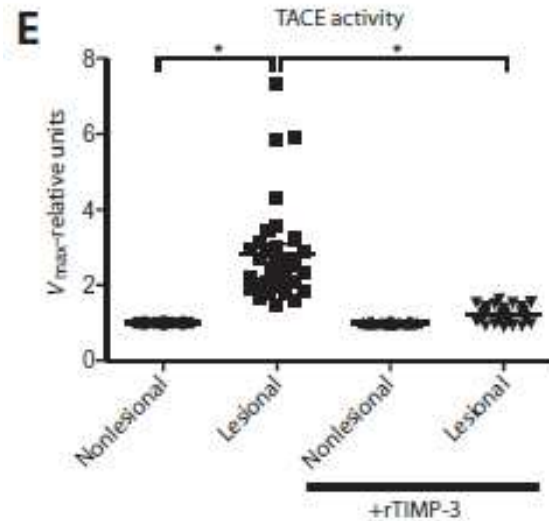
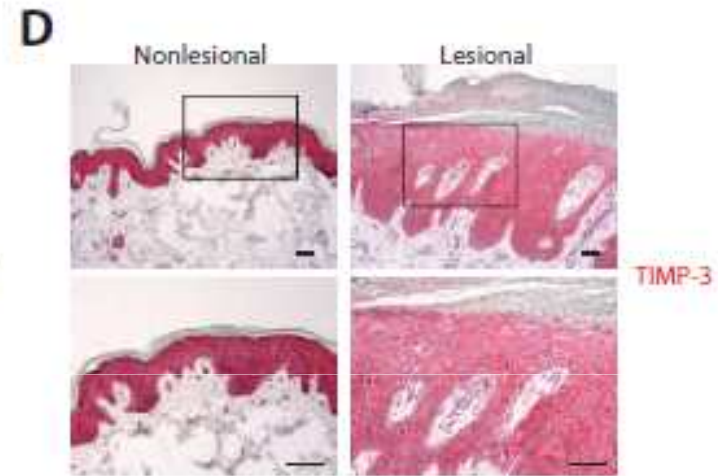


90% correlation

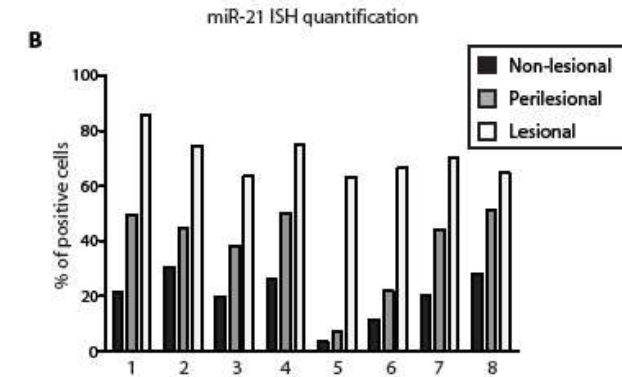
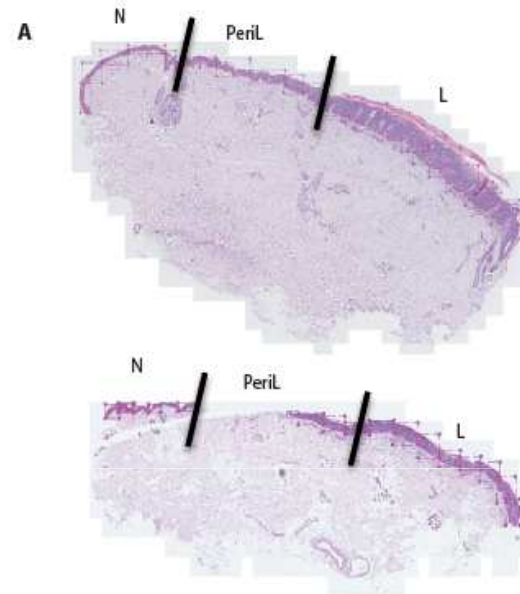
### ISH



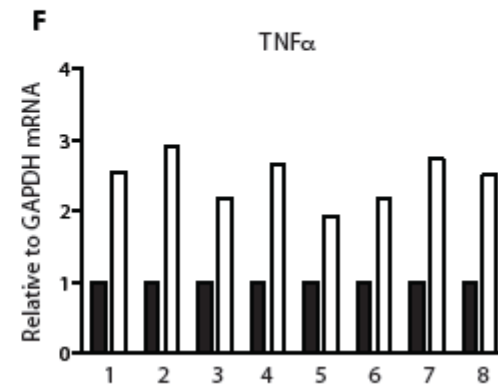
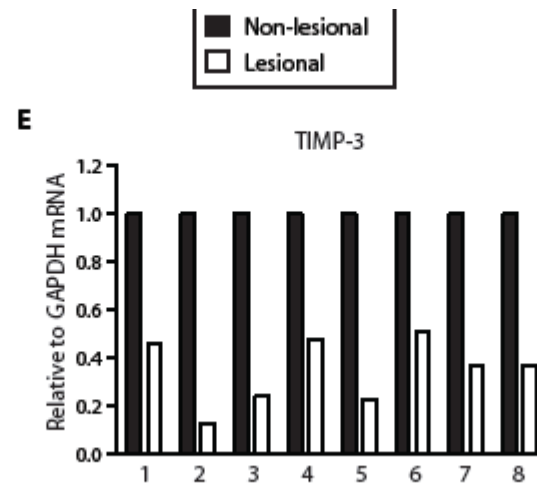
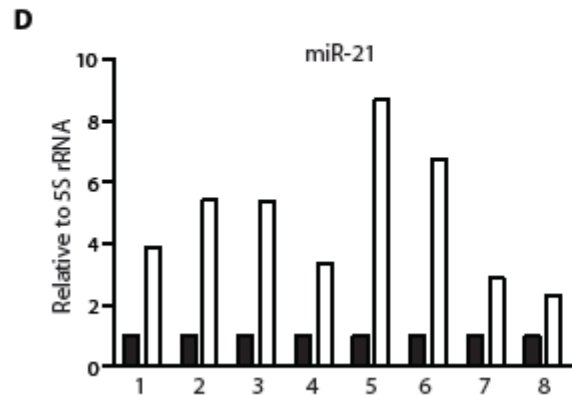
### Immunostaining



**ISH**

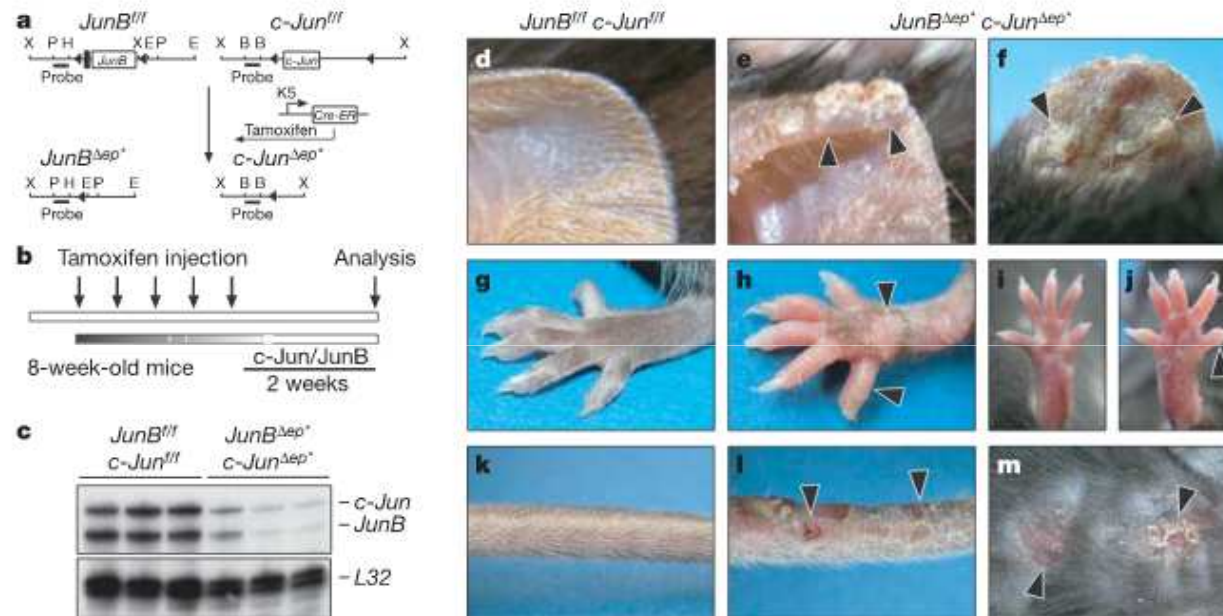


**Epidermal laser capture  
microdissection**





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

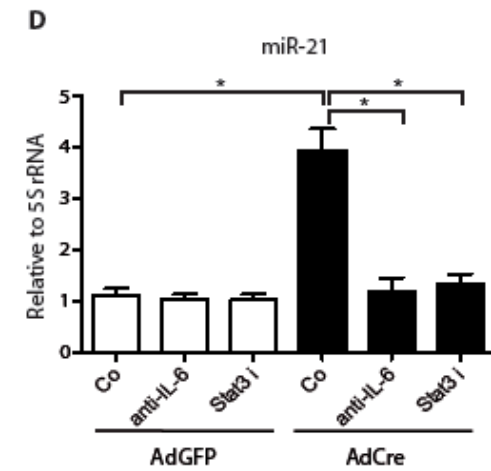
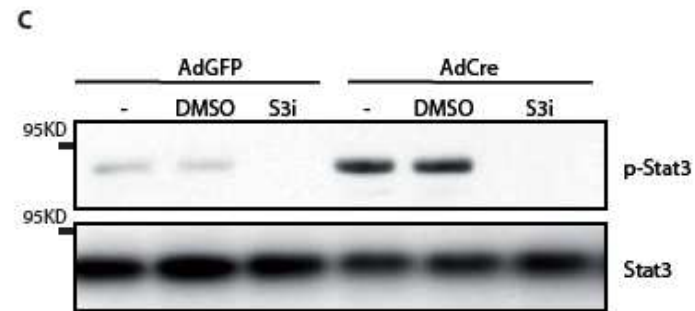
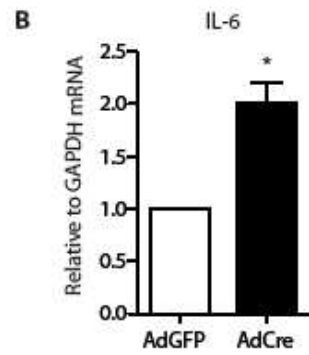
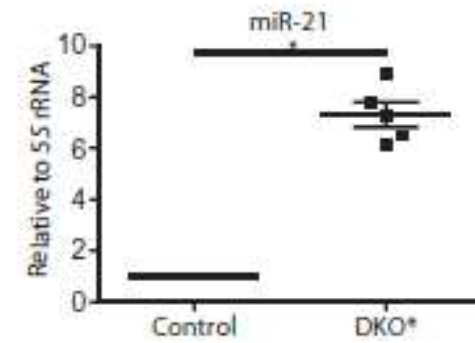
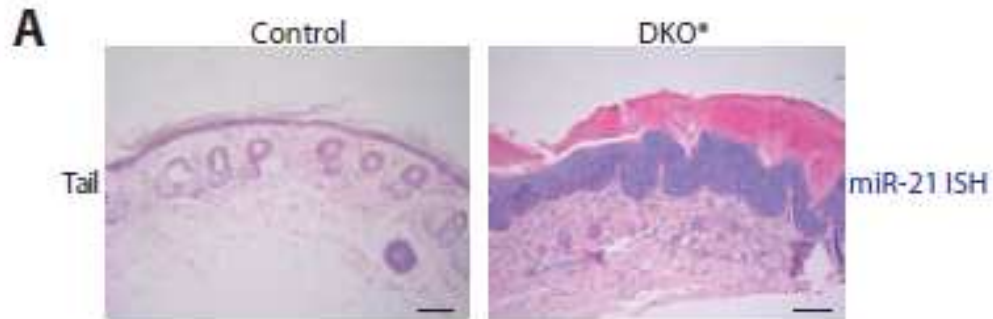


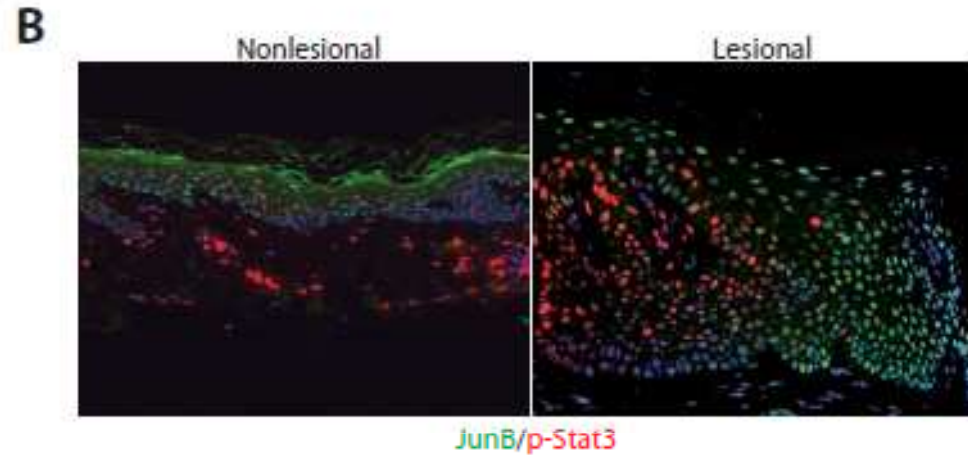
Zenz et al., 2005

The mice mimic human disease in:

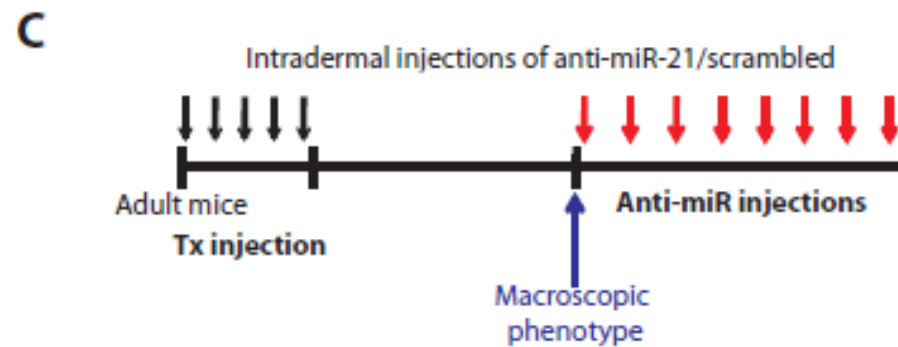
- hyper- and parakeratosis
- leukocyte infiltration
- intraepidermal T cells
- increased angiogenesis
- epidermal microabscesses

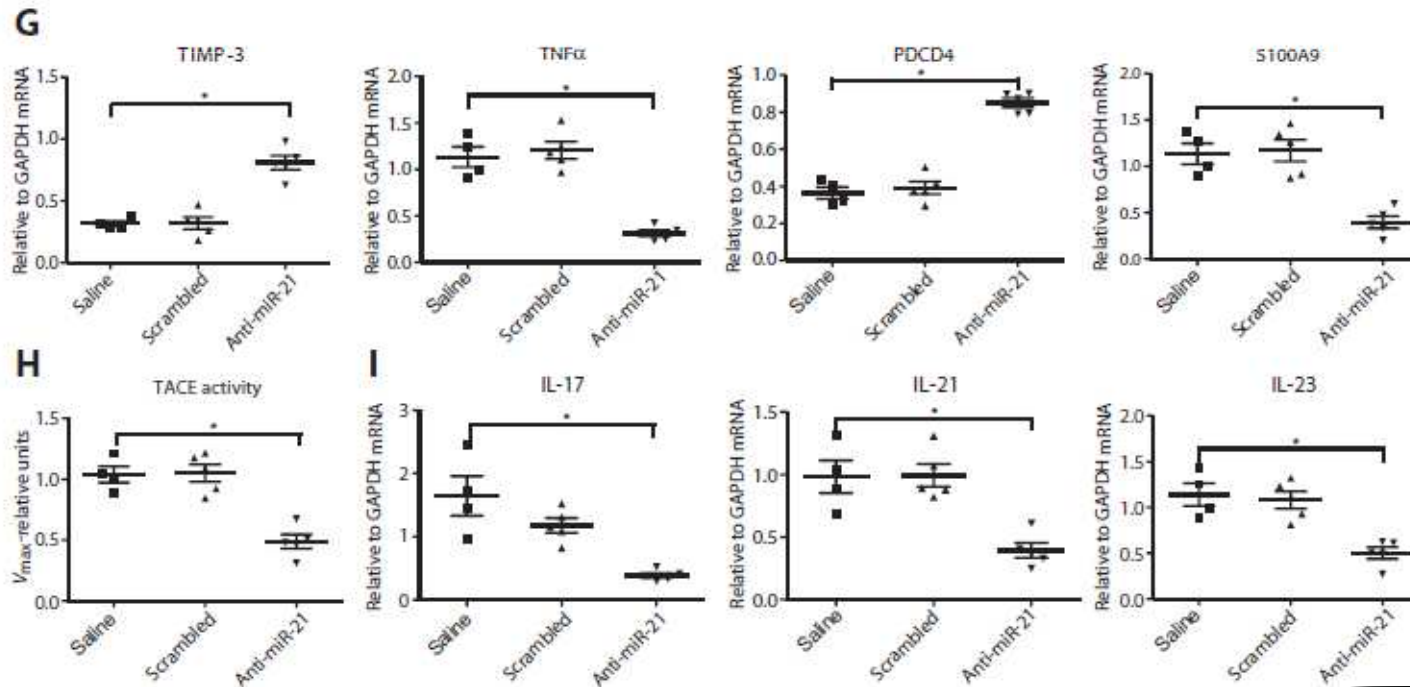
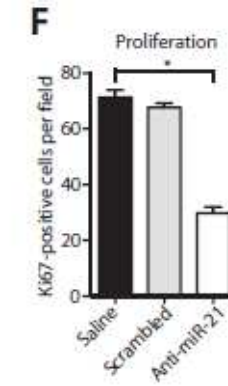
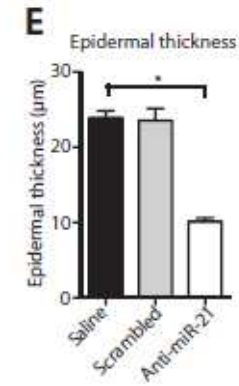
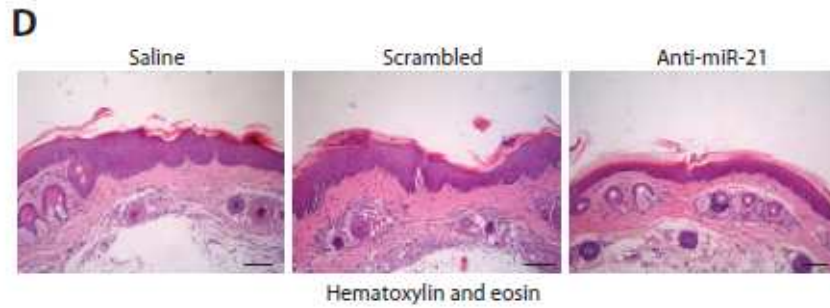
## ISH



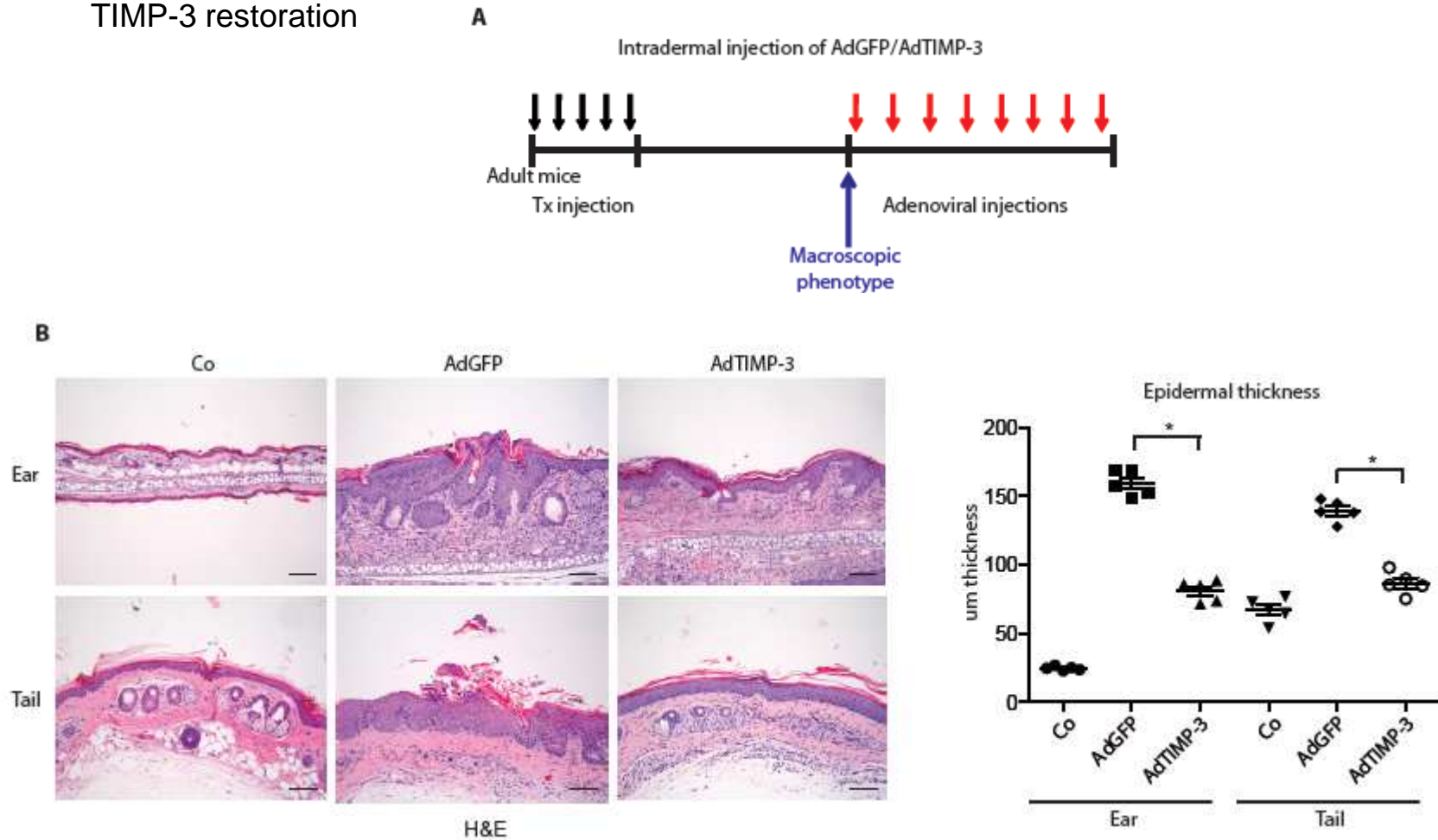


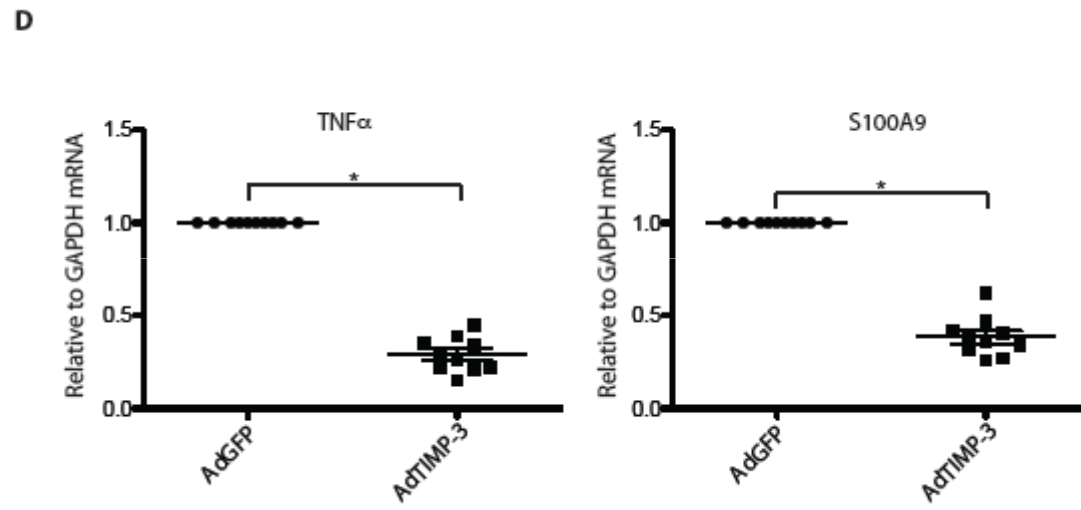
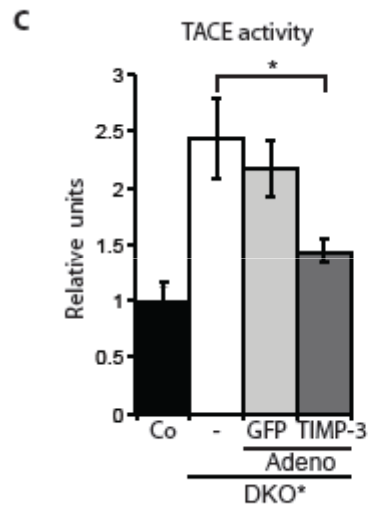
To analyze whether miR-21 has a causal role in psoriasis progression they used anti-miR-21.





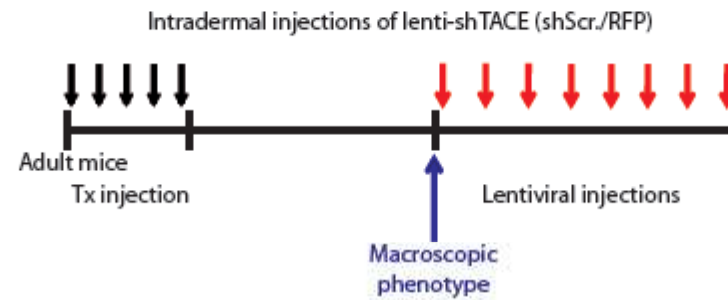
To demonstrate that TIMP-3 are targets of miR-21 in psoriasis, they performed in vivo TIMP-3 restoration



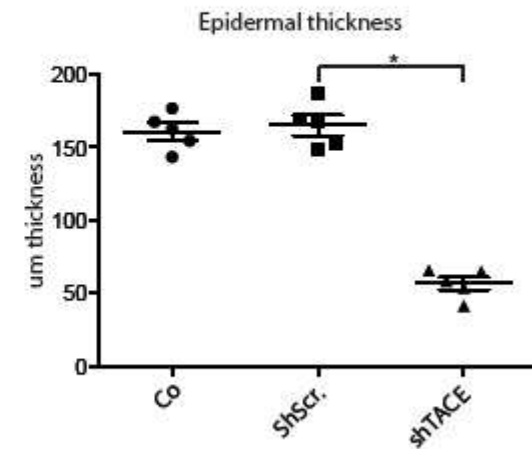
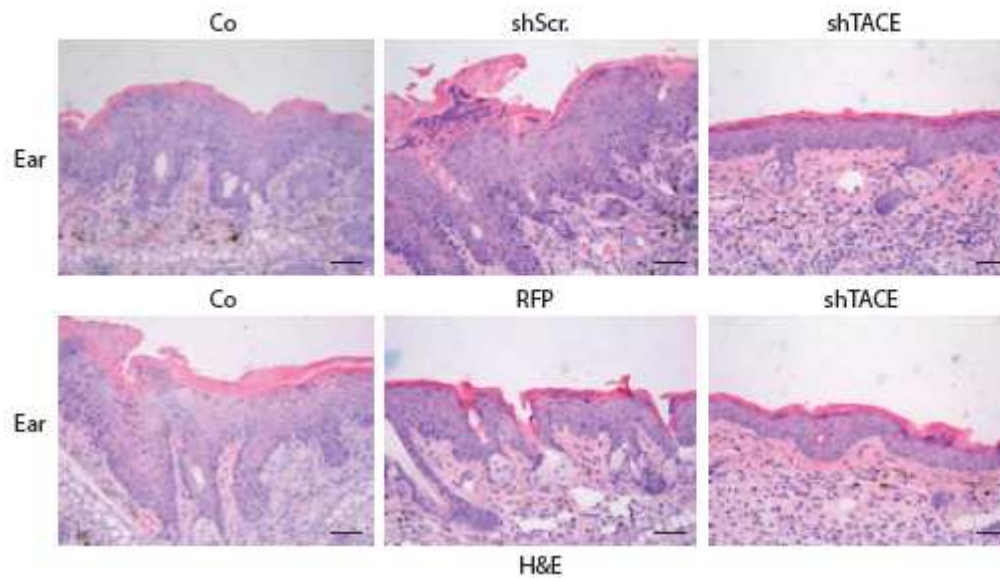


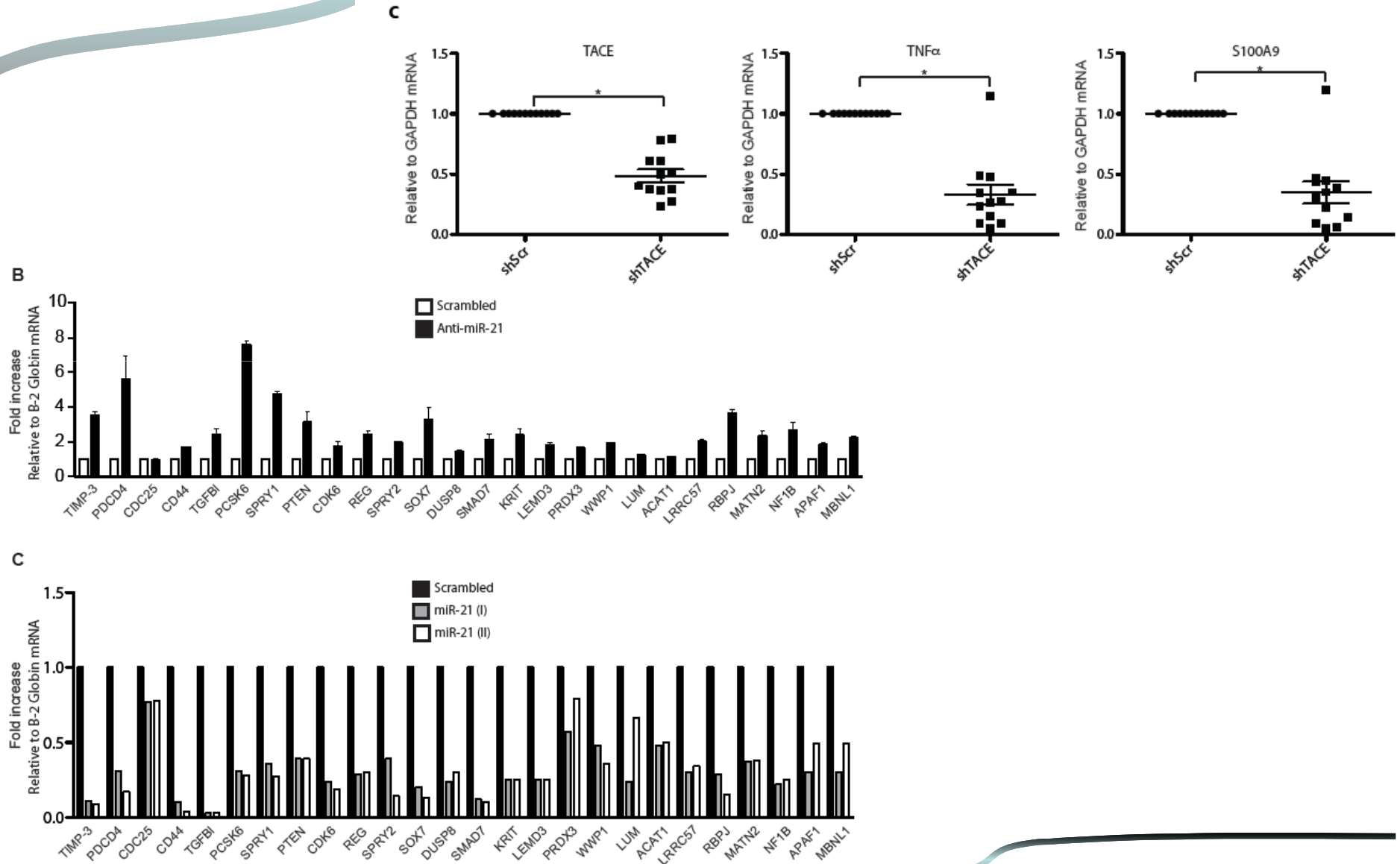
To demonstrate that TACE is a target of miR-21 in psoriasis, they performed in vivo TACE shRNA mediated knockdown

**A**



**B**

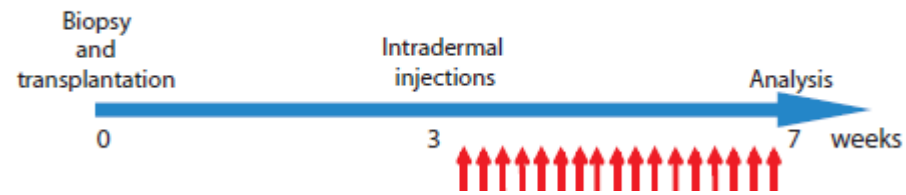




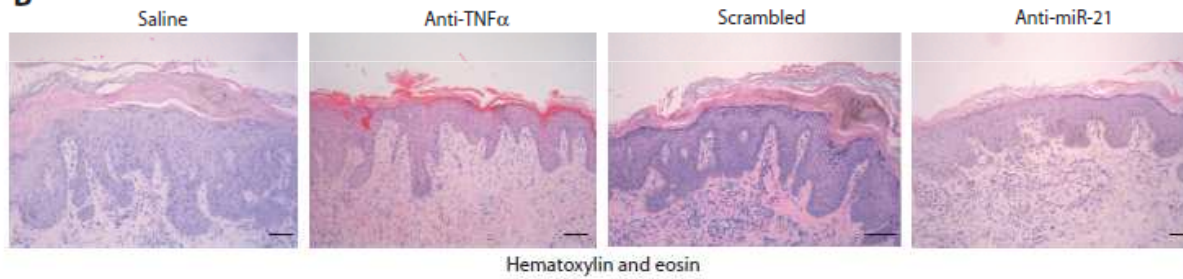


Does miR-21 inhibition has a therapeutic benefit?

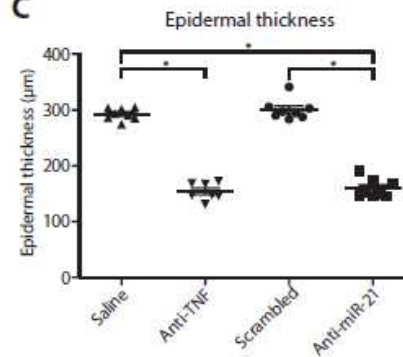
**A**

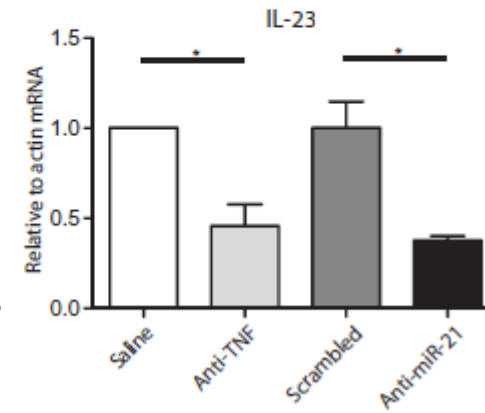
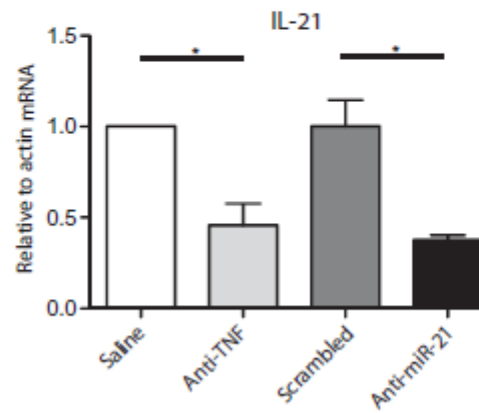
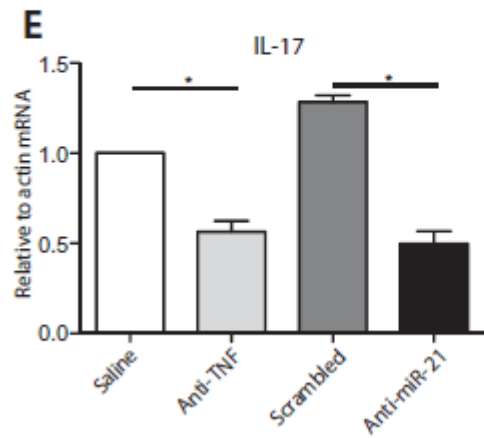
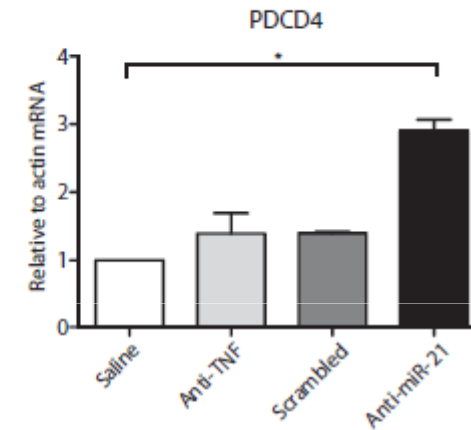
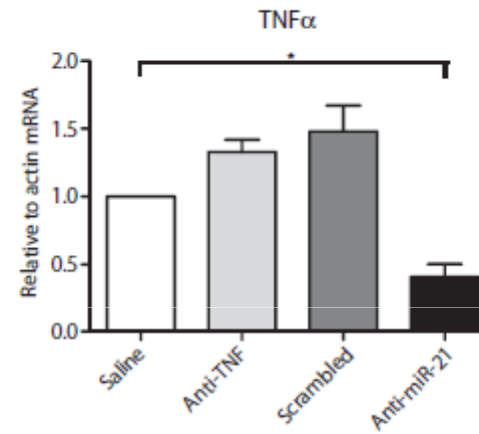
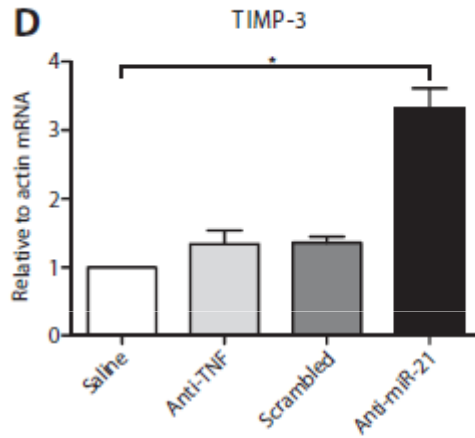


**B**

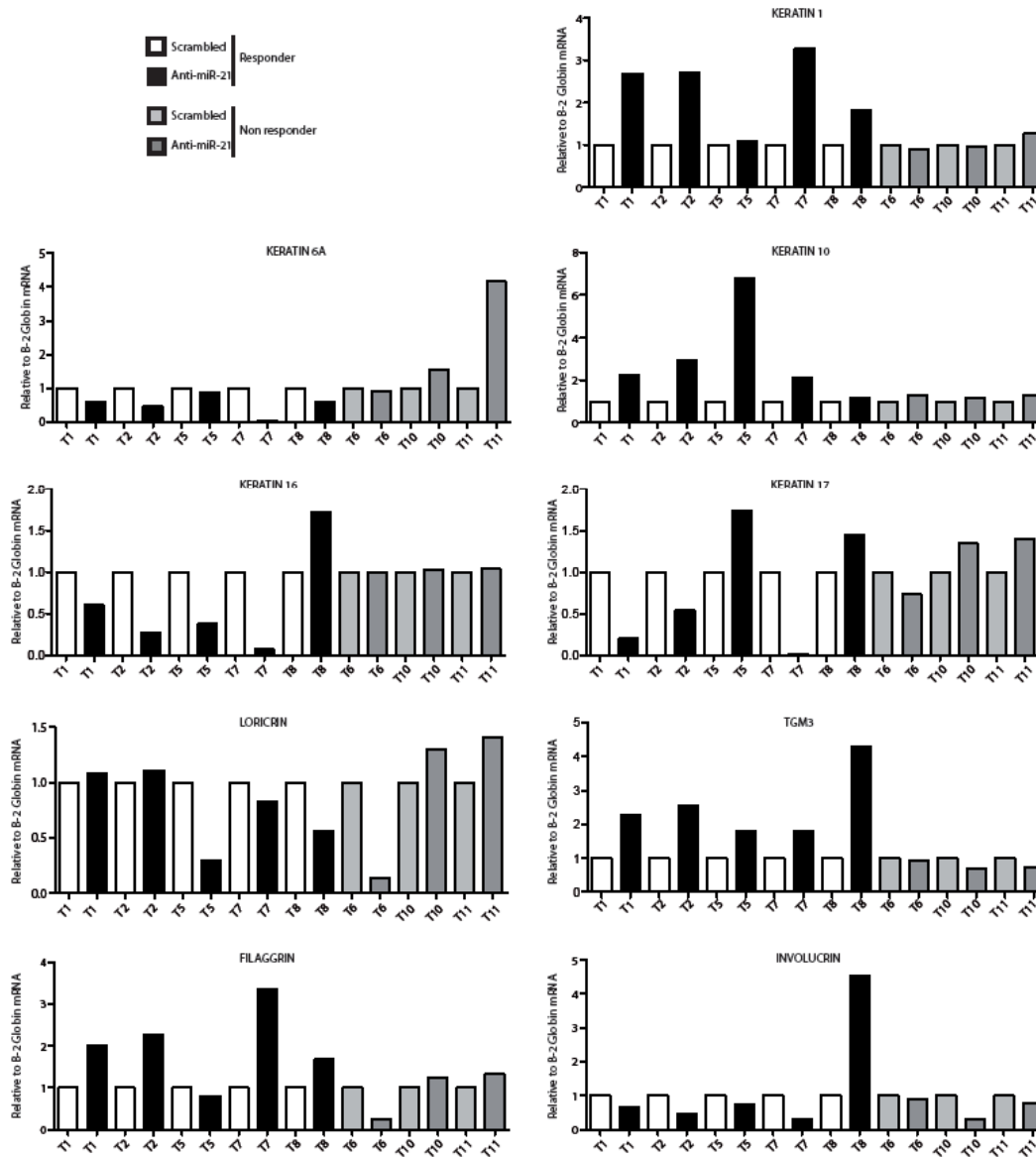


**C**





## Does miR-21 inhibition alter barrier function?



# Summary

