

CMTM4 is a subunit of the IL-17 receptor mediating autoimmune pathology

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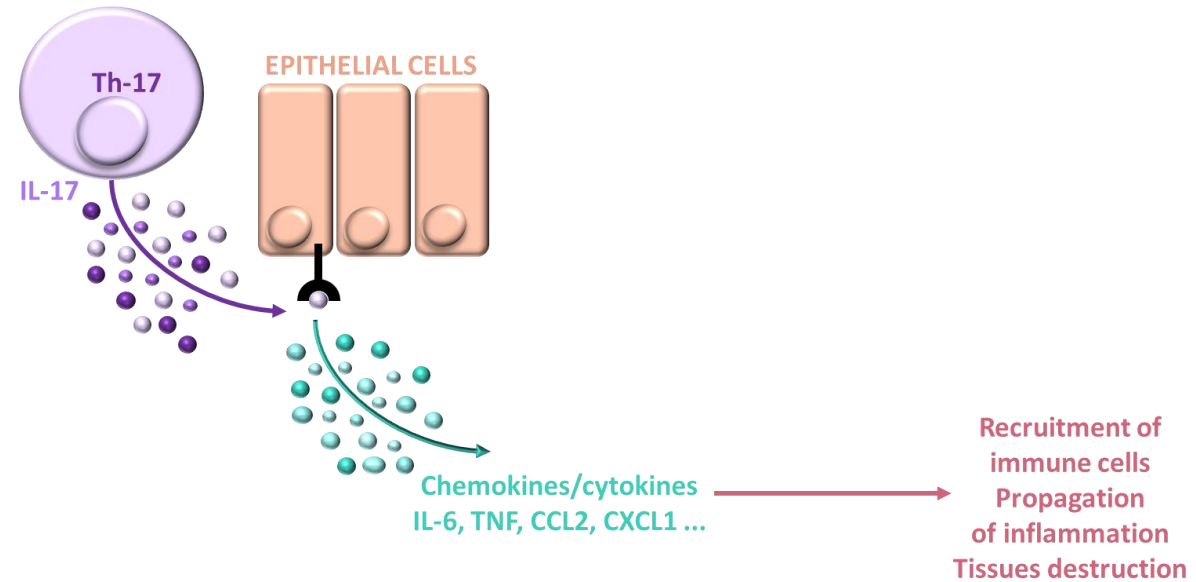


IL-17 – main pro-inflammatory cytokine

Pro-inflammatory cytokine, mainly produced by Th17 cells

Induced expression of pro-inflammatory cytokines such as IL-6, CCL2 or CXCL1

Protects against yeast and bacterial infections
e.g. *Candida Albicans*



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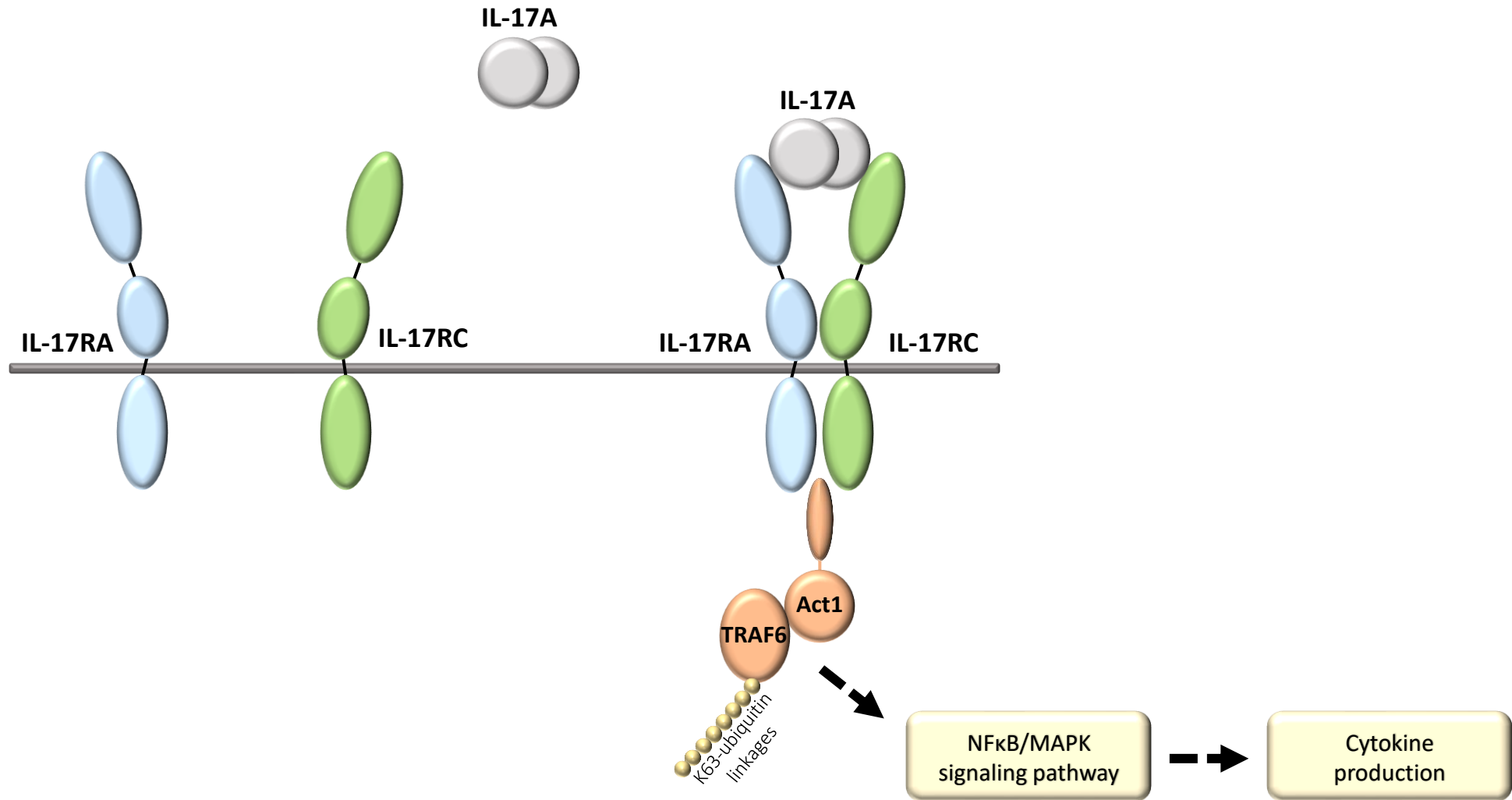
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Dysregulation of IL-17 is associated with a number of autoimmune conditions (rheumatoid arthritis, psoriasis, or multiple sclerosis)

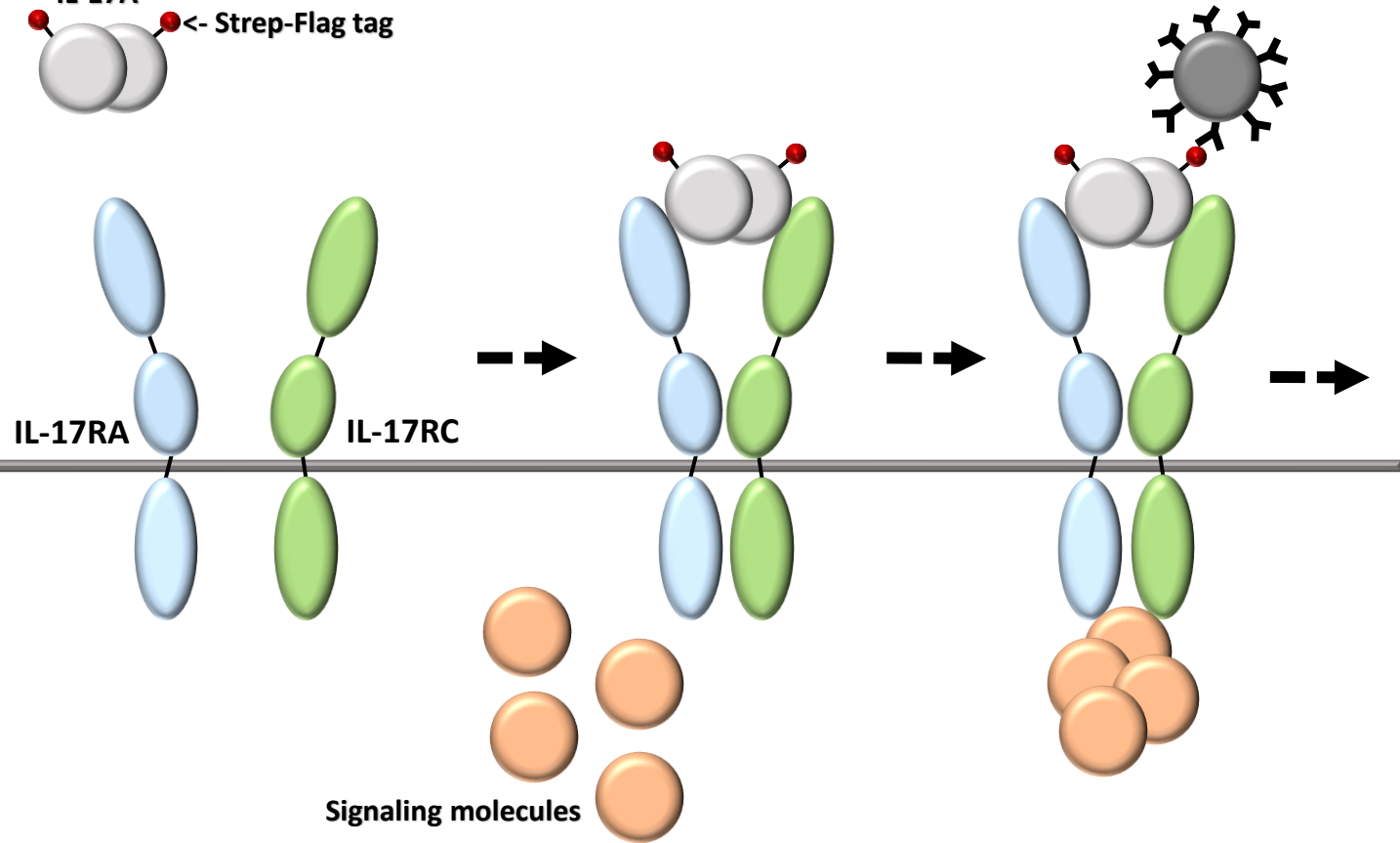


IL-17 – signaling pathway

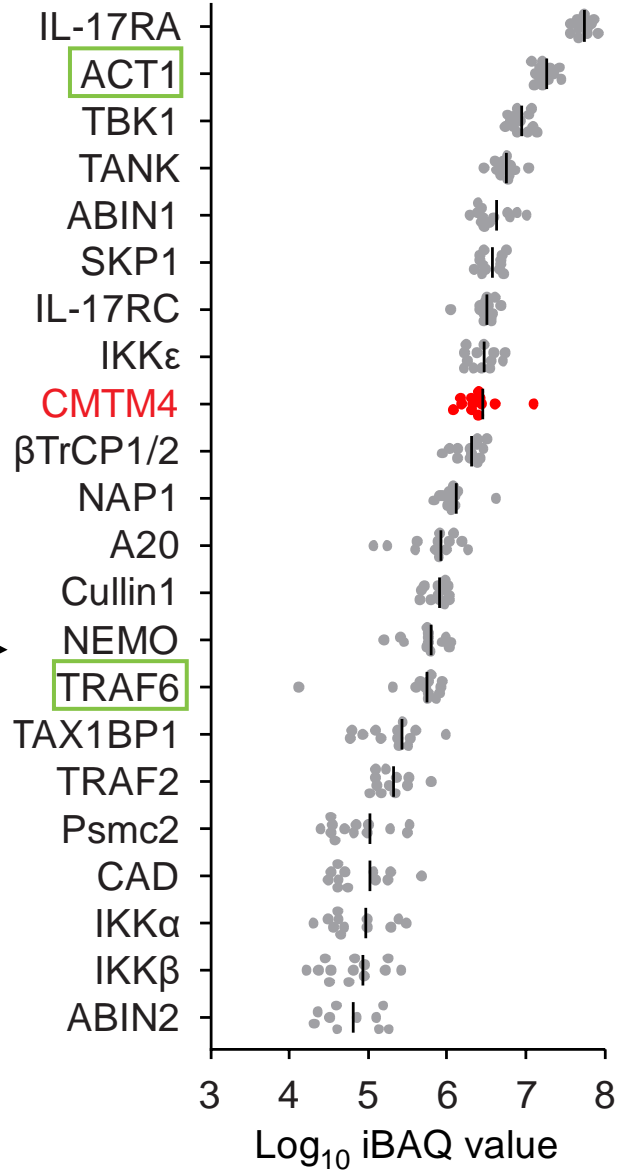


Mass-spec analysis of IL-17 receptor signaling complex

Recombinant
IL-17A
Strep-Flag tag



MS analysis of
proteins recruited to IL-17RSC



Unexpected presence of *CKLF-like MARVEL transmembrane domain containing protein 4* in MS data

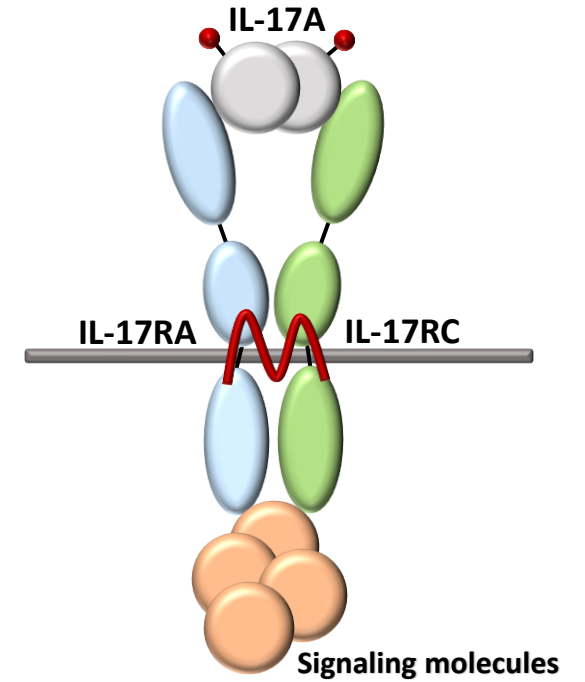
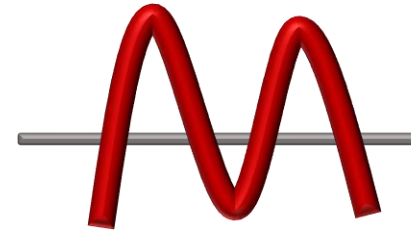
CMTM4 protein

Family of proteins consisting of eight members, CMTM1-8

Transmembrane protein (~ 25 kDa)

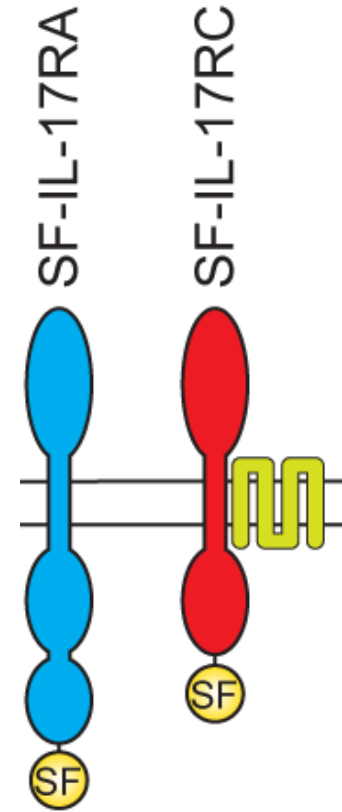
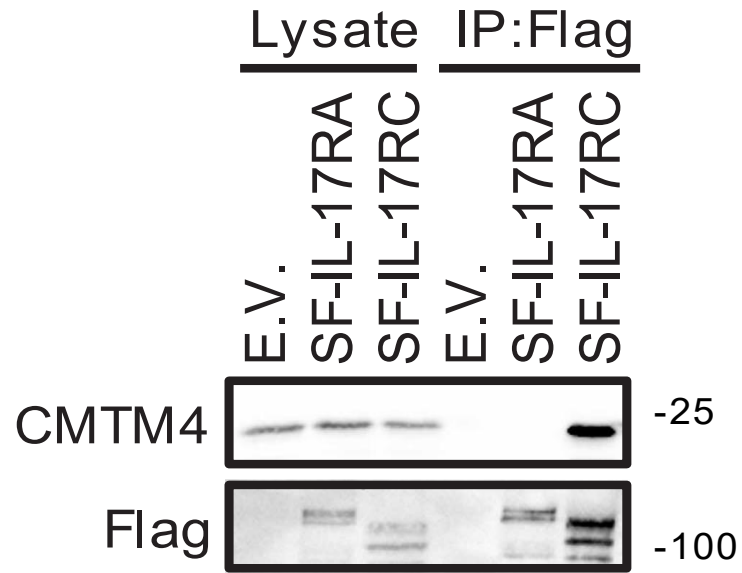
Four-time passing transmembrane domain (helical)

New component of IL-17 receptor signaling complex

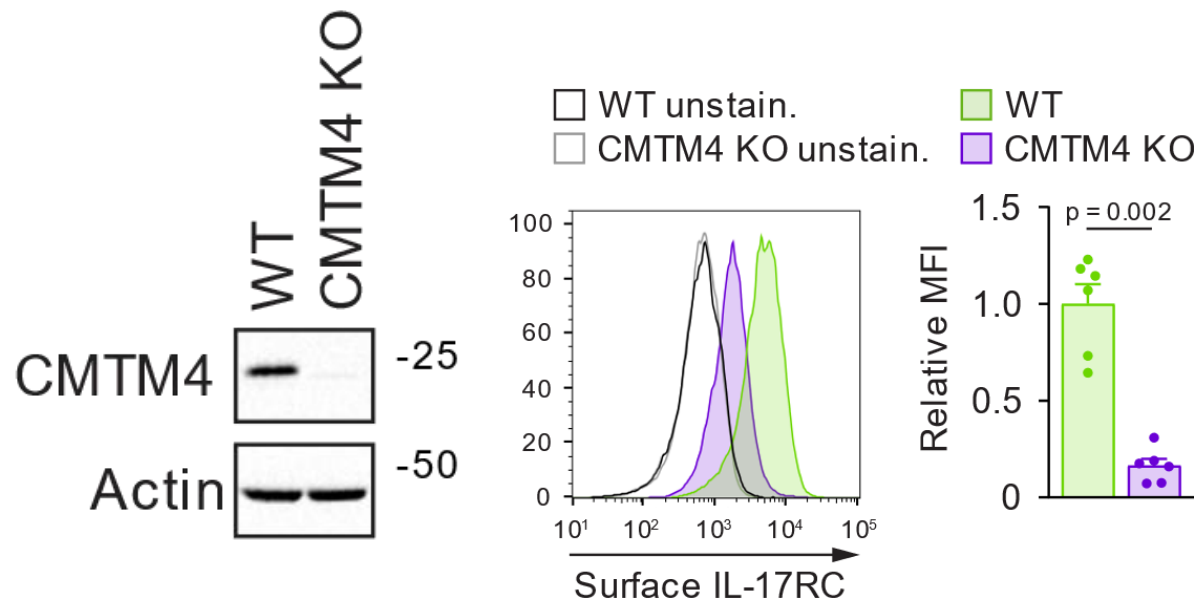


What is the role of CMTM4 within IL-17 receptor signaling complex?

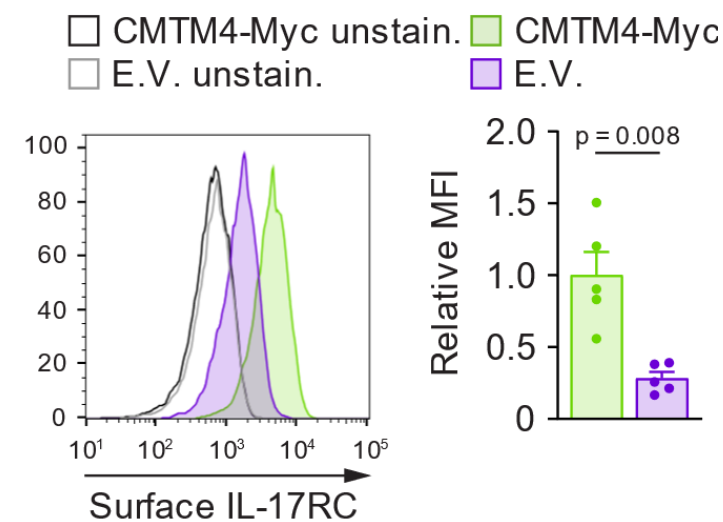
CMTM4 is constitutively associated with IL-17RC



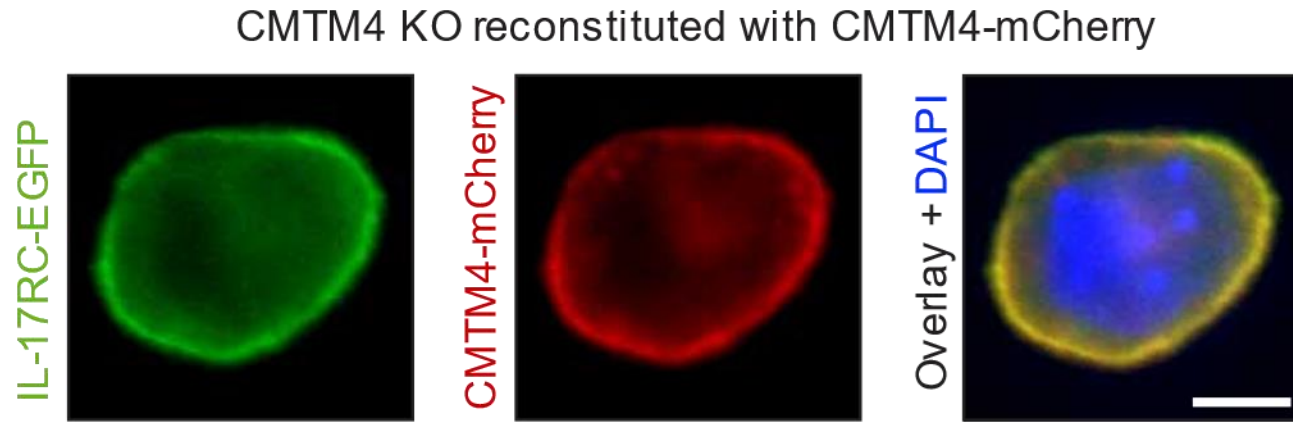
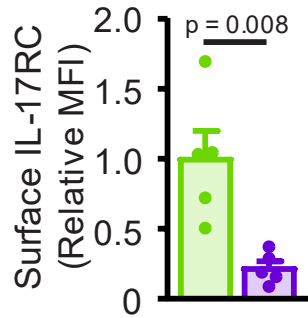
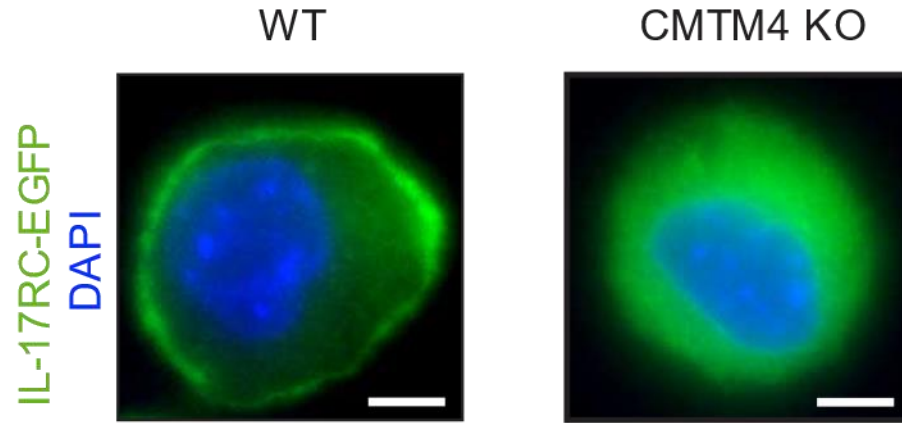
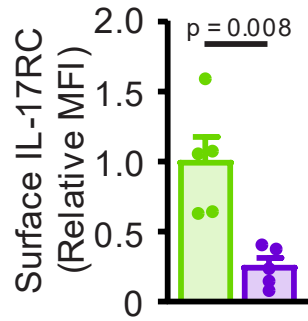
CMTM4 promotes IL-17RC plasma membrane localization



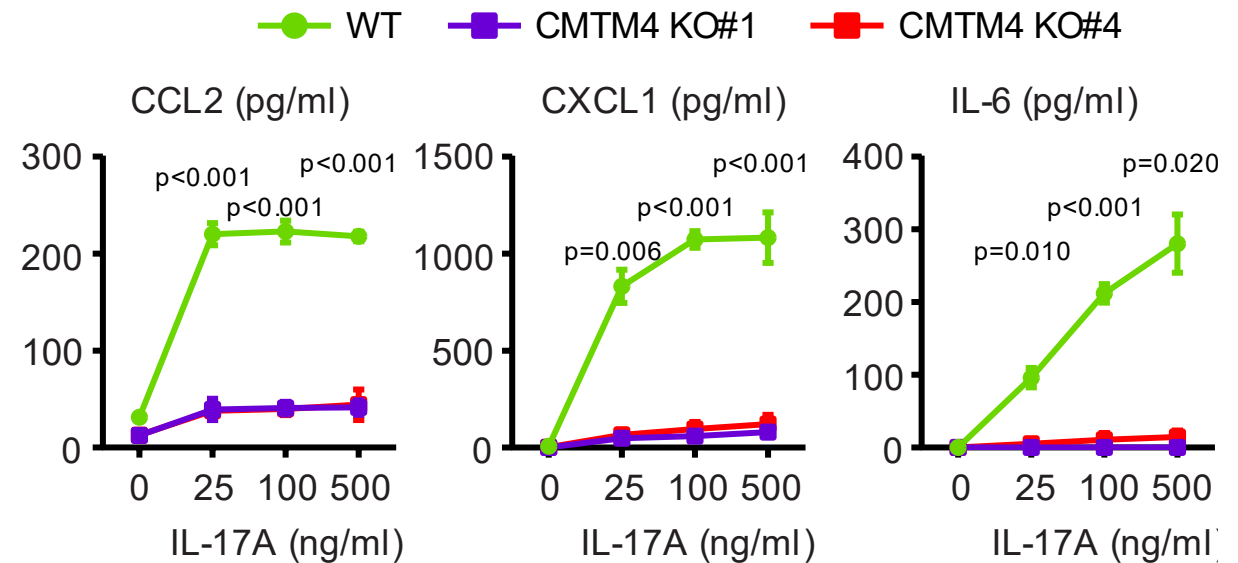
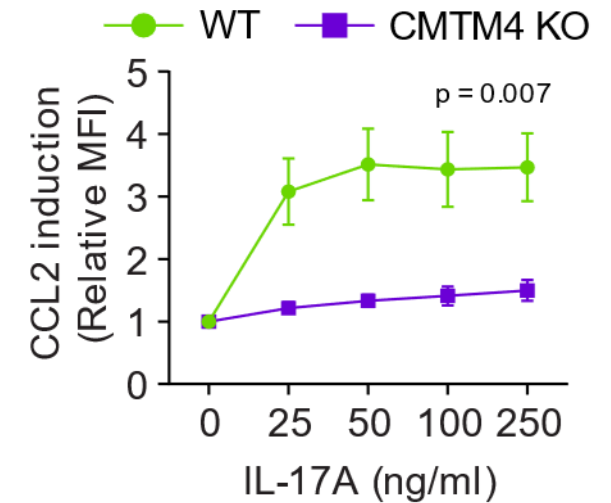
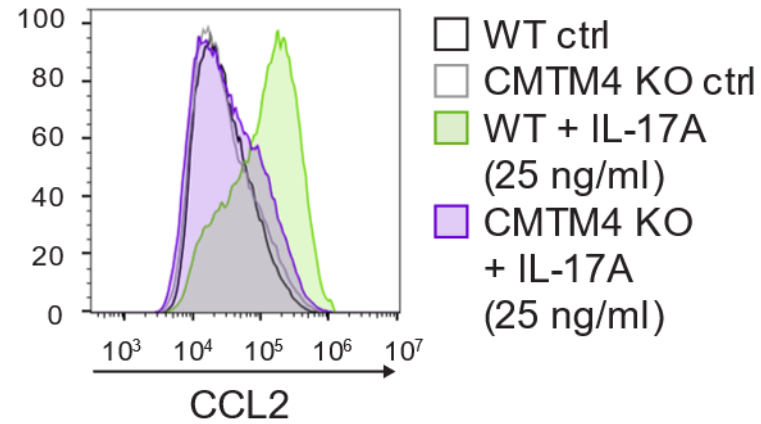
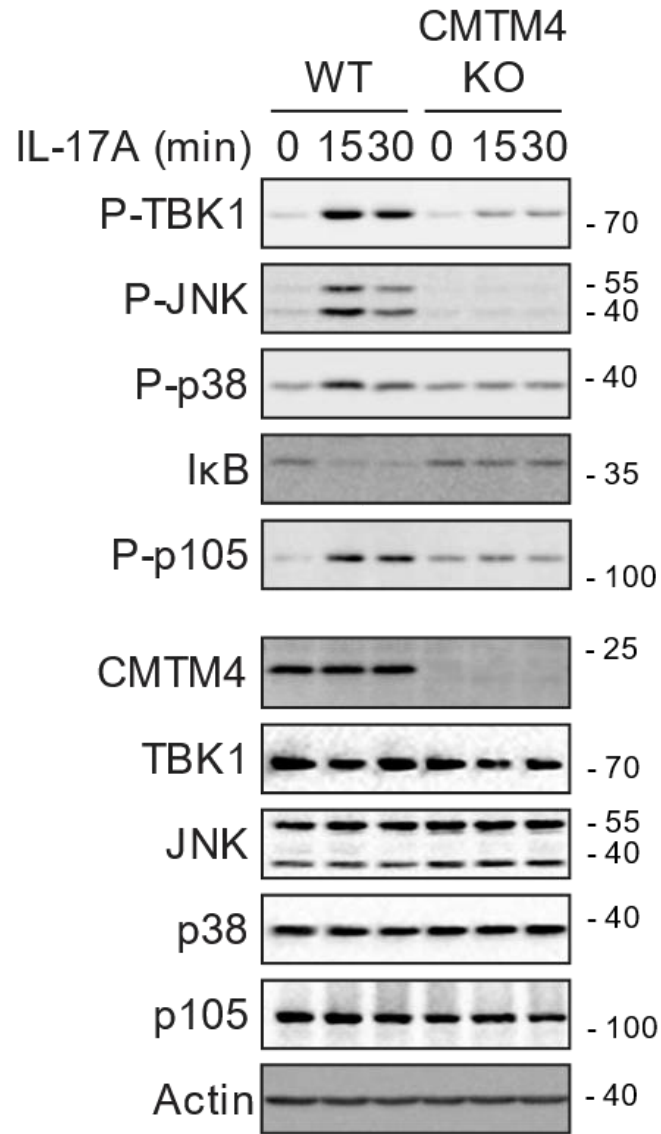
CMTM4 KO reconstituted



CMTM4 promotes IL-17RC plasma membrane localization



CMTM4 is required for IL-17 signaling



CMTM4 is a major regulator of IL-17 signaling *in vivo*

CMTM4 KO mouse

Healthy, no changes in immune cell compartment

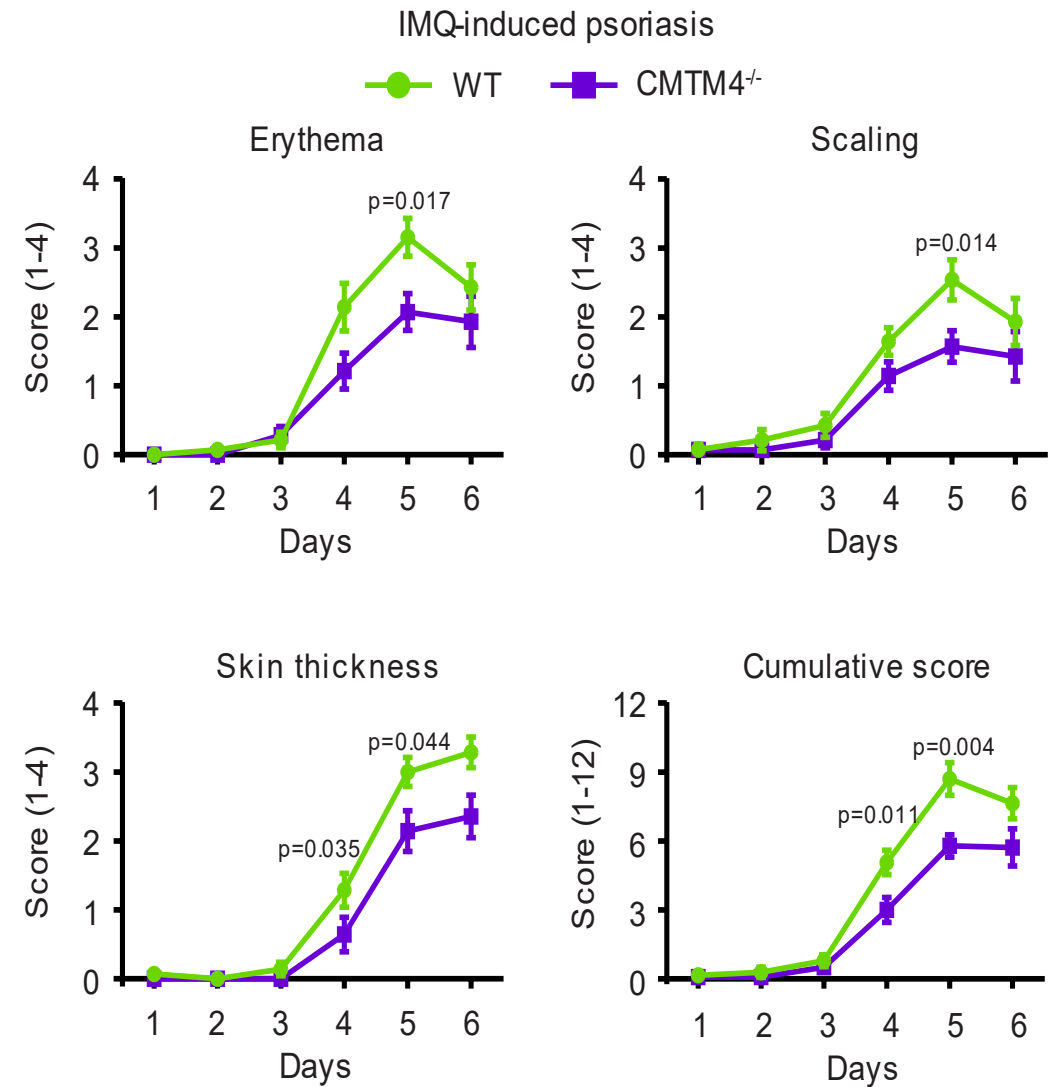
IMQ treatment

Aldara cream containing 5% IMQ was applied on the shaved back skin and the ear daily for five consecutive days

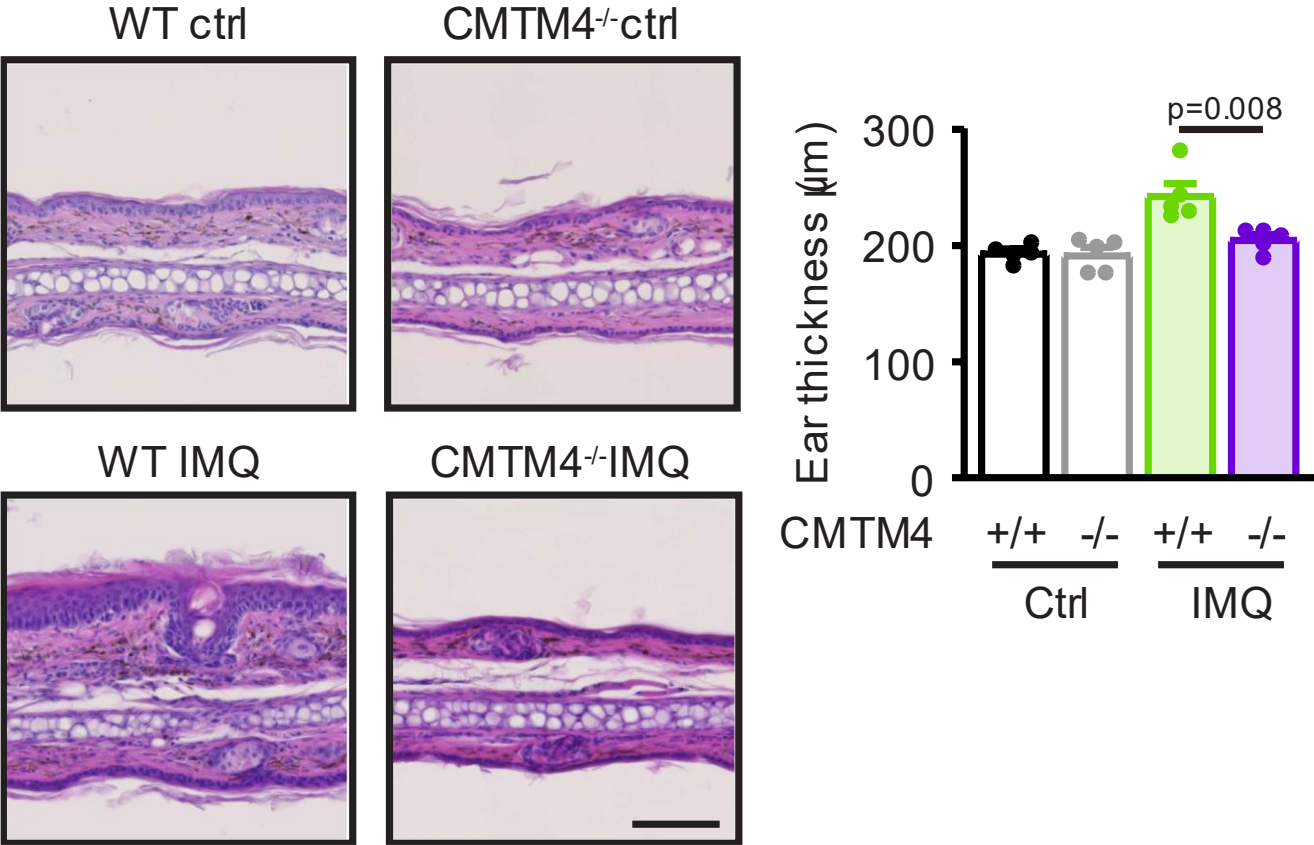
IMQ treatment (day 4)

WT

CMTM4^{-/-}



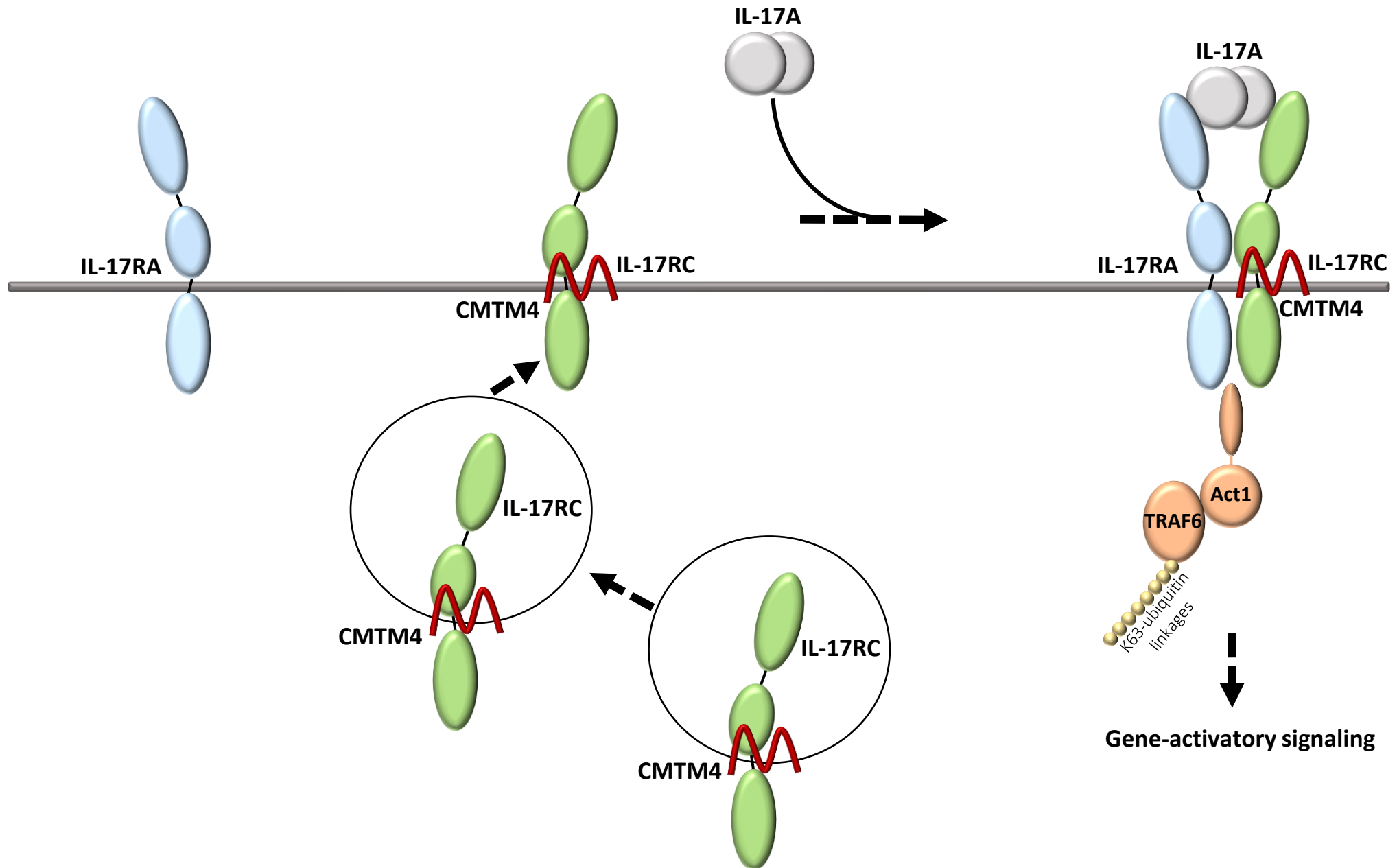
CMTM4 is a major regulator of IL-17 signaling *in vivo*



CONCLUSION

We identified CMTM4 protein as a third subunit of the IL-17 receptor

CONCLUSION



ACKNOWLEDGEMENTS

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PRIMUS



CMTM4 is a new component of IL-17 receptor signaling complex



Thank you for your attention

