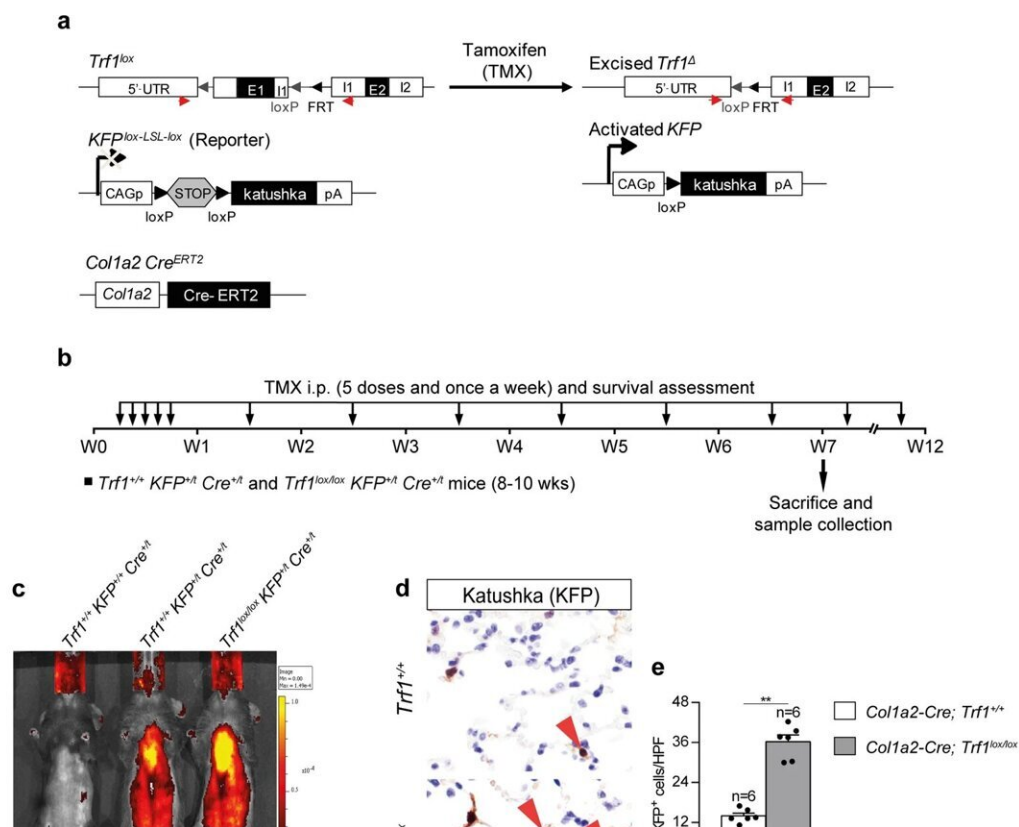


Study: Treatment of pulmonary fibrosis should focus on the telomeres of the cells that regenerate the lungs

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Efficient *Trf1* deletion in lung fibroblasts upon tamoxifen administration. **a** Generation of the conditional knockout mouse model in which *Trf1* was deleted in fibroblasts using the Cre recombinase driven by the *Col1a2* promoter. *Trf1^{lox}*, *KFP^{Lox-LSL-Lox}*, and *Col1a2-Cre^{ERT2}* alleles are depicted before and after Cre-mediated excision. **b** Tamoxifen (TMX) treatment, survival rate assessment and sample collection. Eight-to 10-week-old male *Trf1^{+/+} KFP^{+/-} Cre^{+/-}* (*Col1a2-Cre*;

Trf1^{+/+}) and *Trf1*^{lox/lox} *KFP*^{+/+} *Cre*^{+/+} (*Colla2-Cre*; *Trf1*^{lox/lox}) mice were i.p. injected with TMX for five consecutive days during the first week and once a week until the sacrifice and sample collection on week (W) 7, and during the follow-up of survival until W12. **c** Representative images of fluorescence intensity of katushka fluorescent protein (KFP) in *Trf1*^{+/+} *KFP*^{+/+} *Cre*^{+/+}, *Trf1*^{+/+} *KFP*^{+/+} *Cre*^{+/+} and *Trf1*^{lox/lox} *KFP*^{+/+} *Cre*^{+/+} mice. Representative immunostainings for KFP (**d**), and quantification of KFP positive cells per 40X high-power field (HPF) (**e**) in lung sections from *Trf1*^{+/+} *KFP*^{+/+} *Cre*^{+/+} and *Trf1*^{lox/lox} *KFP*^{+/+} *Cre*^{+/+} mice. **f** Kaplan–Meier survival curves of *Colla2-Cre*; *Trf1*^{+/+} (*Trf1*^{+/+}, controls) and *Colla2-Cre*; *Trf1*^{Δ/Δ} (*Trf1*^{Δ/Δ}) mice upon TMX treatment. **g** Representative immunofluorescence stainings for COL1A2 (green) and TRF1 (red) (white arrowheads indicate COL1A2⁺ fibroblasts with deletion of TRF1), and immune-telomere-Q-FISH in COL1A2⁺ fibroblasts (Cy3Tel probe (red), COL1A2⁺ cells (green), and nuclei stained with DAPI (blue)) in lung sections from *Trf1*^{+/+} and *Trf1*^{Δ/Δ} mice. Quantification of the proportion of double COL1A2⁺-TRF1⁺ fibroblasts (**h**) and mean telomere spot intensity (**i**) and average number of telomeres (**j**) in COL1A2⁺ cells from *Trf1*^{+/+} and *Trf1*^{Δ/Δ} mice. Data are expressed as mean ± SEM (the number of mice is indicated in each case). ***p*

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