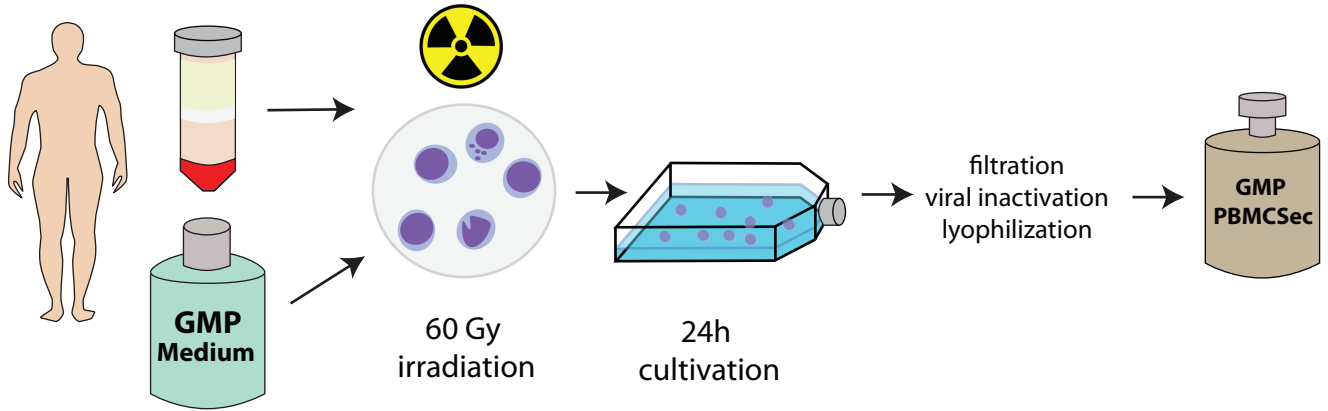


(A)



(B)

PBMC isolation

Target	Supplier	Product Nr.	Host species	Dilution	Application
GAPDH	abcam	ab8245	mouse monoclonal	1:10000	WB
Collagen I	abcam	ab34710	rabbit polyclonal	1:200	IF
Collagen III	abcam	ab7778	rabbit polyclonal	1:200	IF
Elastin	Merck	Mab2503	mouse monoclonal	1:100	IF, WB
Alexa fluor® 546 anti-mouse IgG (H + L)	Invitrogen	A-11030	goat polyclonal	1:500	IF, 2nd step
Alexa fluor® 546 anti-rabbit IgG (H + L)	Invitrogen	A-11035	goat polyclonal	1:500	IF, 2nd step
Anti-mouse, HRP-conjugated	GE Healthcar	GENX-A931	goat polyclonal	1:10 000	WB, 2nd step
Anti-rabbit, HRP-conjugated	Bio-Rad	#1706511	goat polyclonal	1:10 000	WB, 2nd step

Figure S1: Methods

A) Workflow of GMP-PBMCsec-production: leukocyte cones are obtained as blood-donation by-product, PBMCs are isolated by Ficoll-centrifugation, cells are irradiated with 60Gy and incubated for 24h. Superantatants are filtrated and lyophilized, and off-the-shelf PBMCsec is stored at -20° until use.

B) Table of antibodies used. IF = immunofluorescence, WB = western blot

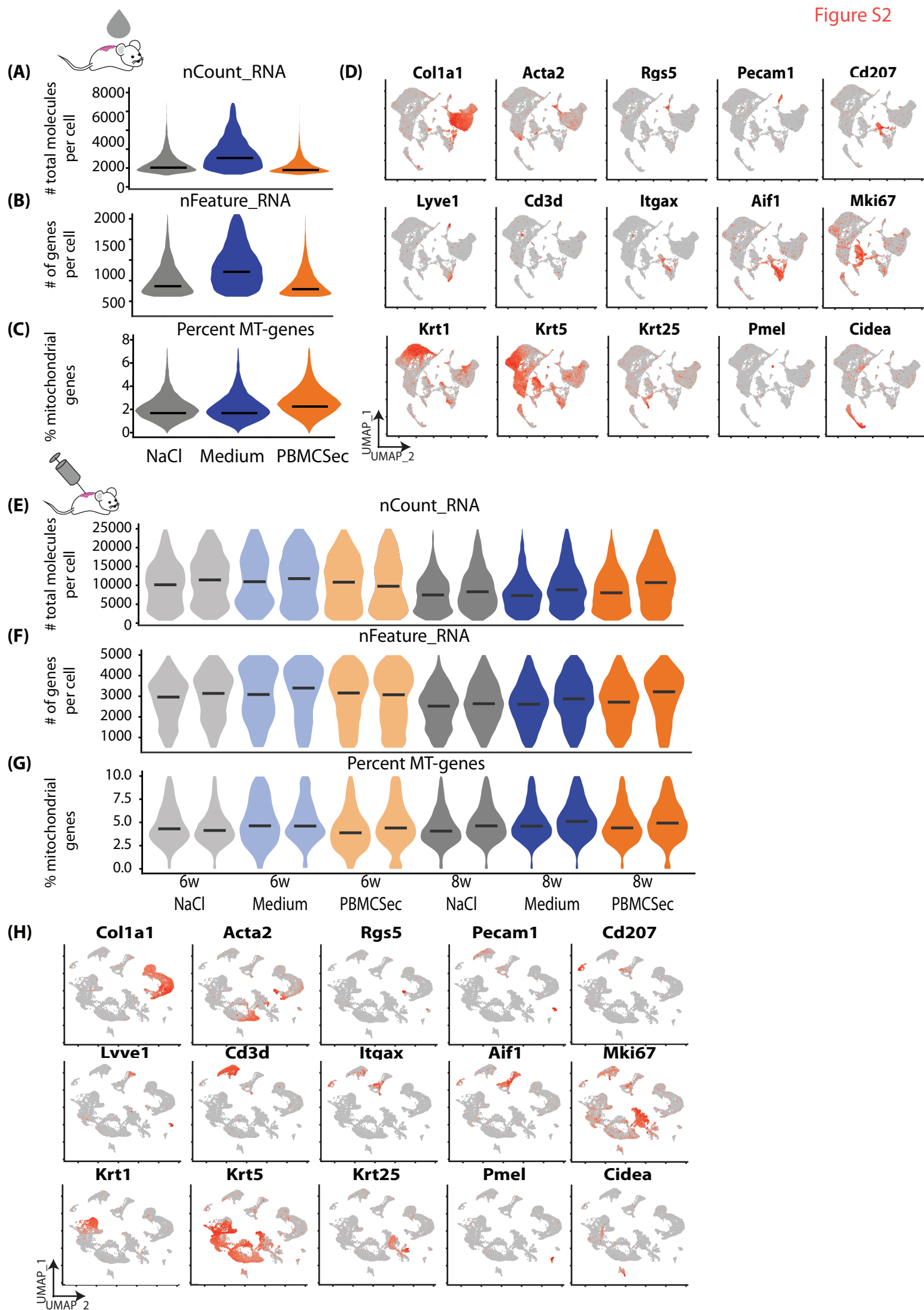


Figure S2: Quality control of mouse scRNAseq

A-C, E-G) Violin plots of quality control parameters of the 'topical' and 'inject' dataset. A, E) total molecules per cell B, F) (gene count per cell and C, G) mitochondrial gene content. D, H) Feature Plots of cluster markers for cluster identification in the 'topical' and 'inject' dataset: *Col1a1* (collagen I alpha 1) for fibroblasts, *Acta2* (smooth muscle actin) for smooth muscle cells and myofibroblasts, *Rgs5* (Regulator Of G Protein Signaling 5) for pericytes, *Pecam* (Platelet And Endothelial Cell Adhesion Molecule 1) for endothelial cells, *Lyve1* (Lymphatic Vessel Endothelial Hyaluronan Receptor 1) for lymphatic endothelial cells, *Cd207* (Langerin) for Langerhans cells, *Cd3d* (cluster of differentiation 3D) for T-cells, *Itgax* for dendritic cells, *Aif1* (allograft inflammatory factor 1) for macrophages, *Mki67* (Marker Of Proliferation Ki-67) for proliferating cells, *Krt1* (Keratin1) for spinous and granular keratinocytes (KCs), *Krt5* (Keratin 5) for basal KCs, *Krt25* (Keratin 25) for hair follicles, *Pmel* (Premelanosome Protein) for melanocytes, *Cidea* (Cell Death Inducing DFFA Like Effector A) for adipocytes. Vertical lines in violin plots represent maximum expression, shape of each violin represents all results, and width of each violin represents frequency of cells at the respective expression level. In feature plots, normalized log expression of the respective gene is mapped onto the UMAP-plot. Color intensity indicates level of gene expressions. UMAP, uniform manifold approximation and projection.



Figure S3

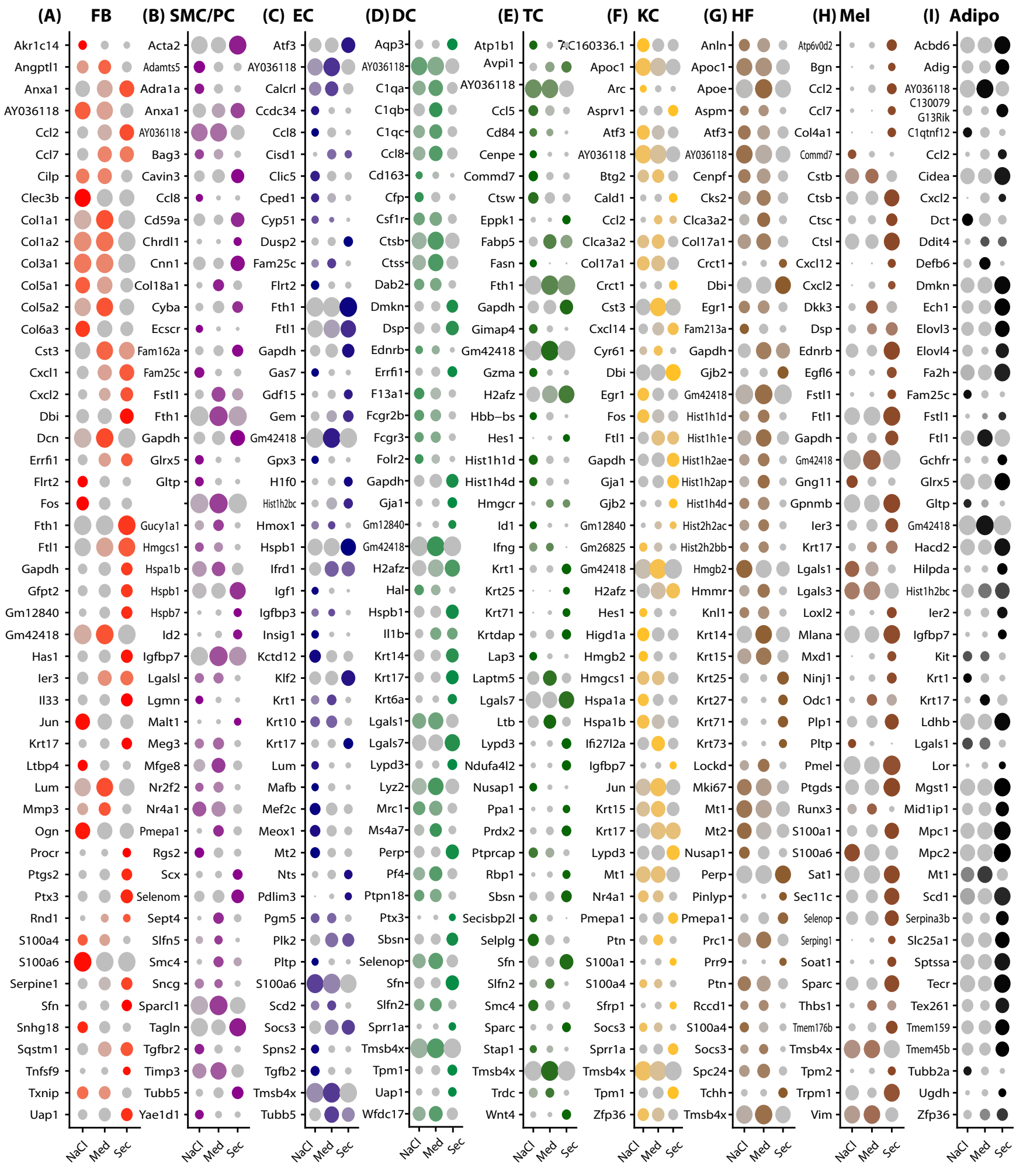


Figure S3: Top 50 regulated genes per cell group in 'Topical' mouse scars

In A) fibroblasts (FBs, red circles), B) smooth muscle cells and pericytes (SMC/PCs, purple), C) endothelial cells (ECs, blue), D) T-cells (dark green), E) dendritic cells and macrophages (DCs, light green), and keratinocytes (KCs, yellow), hair follicles (HF, beige), melanocytes (Mel, brown), adipocytes (Adipo, grey); differentially expressed genes (DEGs) were calculated comparing 'PBMsec' mouse scars to 'NaCl'-mouse scars, using Wilcoxon rank sum test, including genes with average logarithmic fold change (avglogFC) of > 0.1 or < -0.1 and Bonferroni-adjusted p-value < 0.05 . For each cellgroup, top 50 DEGs according to lowest adjusted p-value are displayed, split by treatment. Dot size represents percent of cells expressing the respective gene, color correlates with average expression.

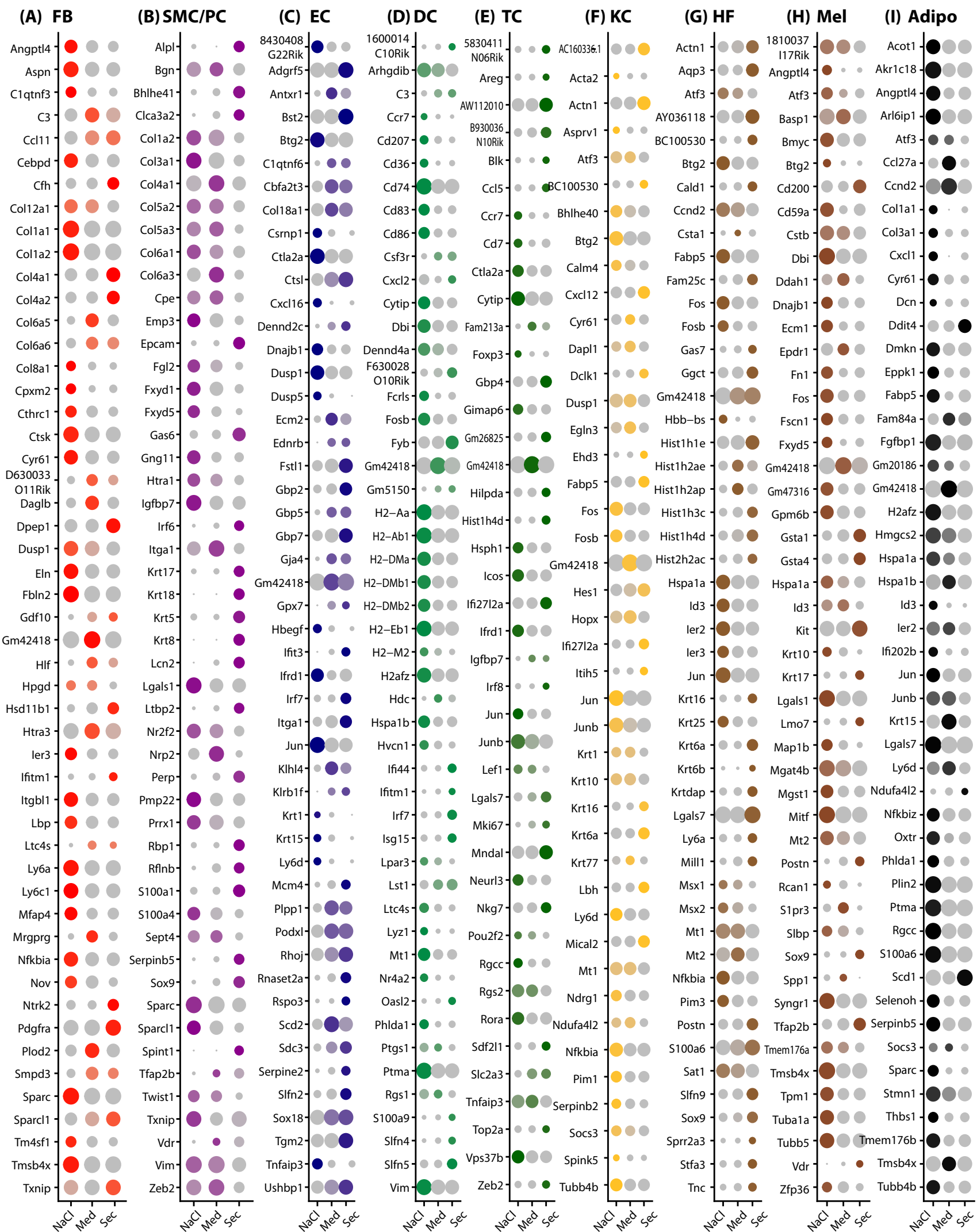


Figure S4: Top 50 regulated genes per cell group in 6 weeks 'Inject' mouse scars

In A) fibroblasts (FBs, red circles), B) smooth muscle cells and pericytes (SMC/PCs, purple), C) endothelial cells (ECs, blue), D) T-cells (dark green), E) dendritic cells and macrophages (DCs, light green), and keratinocytes (KCs, yellow), hair follicles (HF, beige), melanocytes (Mel, brown), adipocytes (Adipo, grey); differentially expressed genes (DEGs) were calculated comparing 'PBMsec' mouse scars to 'NaCl'-mouse scars, using Wilcoxon rank sum test, including genes with average logarithmic fold change (avglogFC) of > 0.1 or < -0.1 and Bonferroni-adjusted p-value < 0.05 . For each cellgroup, top 50 DEGs according to lowest adjusted p-value are displayed, split by treatment and timepoint. Dot size represents percent of cells expressing the respective gene, color correlates with average expression.

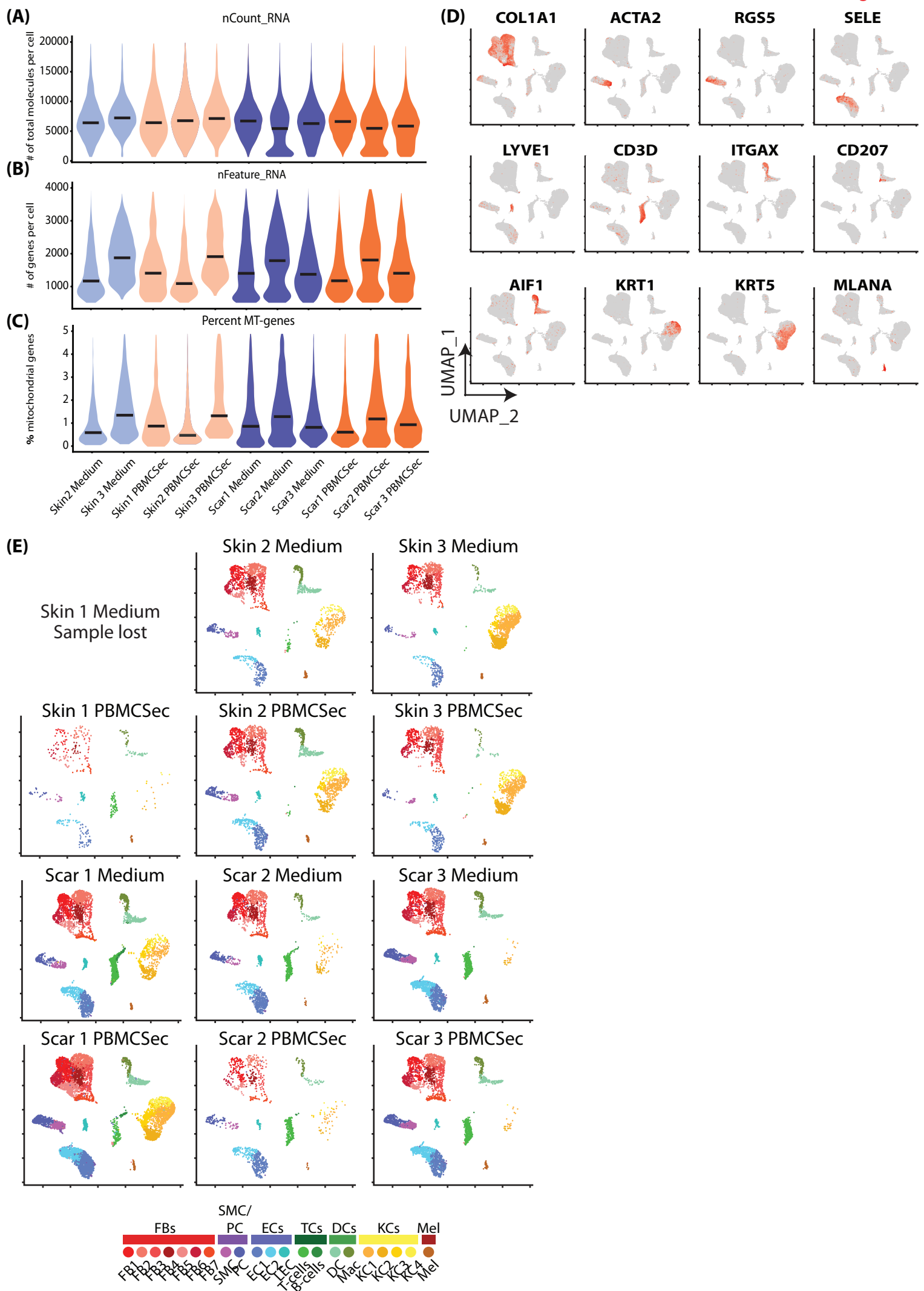


Figure S5: Quality control of human scRNAseq

A-C) Violin plots of quality control parameters of the 'human' dataset. A) total molecules per cell B) (gene count per cell and C) mitochondrial gene content. D) Feature Plots of cluster markers for cluster identification in the 'topical' and 'inject' dataset: *COL1A1* (collagen I alpha 1) for fibroblasts, *ACTA2* (smooth muscle actin) for smooth muscle cells and myofibroblasts, *RGS5* (Regulator Of G Protein Signaling 5) for pericytes, *SELE* (Selectin E) for endothelial cells, *LYVE1* (Lymphatic Vessel Endothelial Hyaluronan Receptor 1) for lymphatic endothelial cells, *Cd3d* (cluster of differentiation 3D) for T-cells, *ITGAX* for dendritic cells, *CD207* (Langerin) for Langerhans cells, *AIF1* (allograft inflammatory factor 1) for macrophages, *KRT1* (Keratin1) for spinous and granular keratinocytes (KCs), *KRT5* (Keratin 5) for basal KCs, *MLANA* (Melan-A) for melanocytes. E) UMAP-clustering in the 'human' dataset, split by samples. Sample "Skin 1 medium" was lost due to technical difficulties during preparation. Vertical lines in violin plots represent maximum expression, shape of each violin represents all results, and width of each violin represents frequency of cells at the respective expression level. In feature plots, normalized log expression of the respective gene is mapped onto the UMAP-plot. Color intensity indicates level of gene expressions. UMAP, uniform manifold approximation and projection

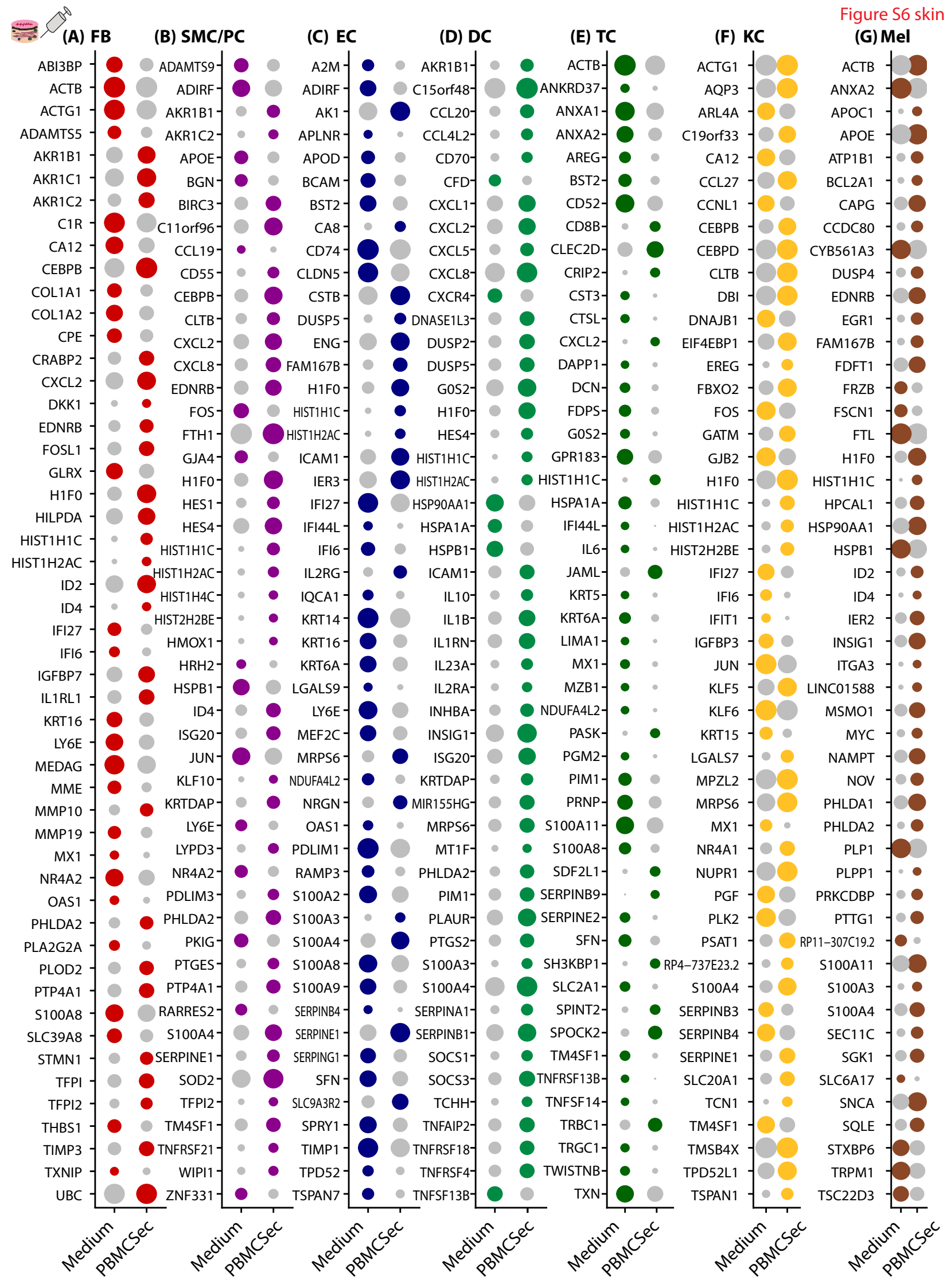


Figure S6: Top 50 regulated genes per cell group in human skin

In A) fibroblasts (FBs, red circles), B) smooth muscle cells and pericytes (SMC/PCs, purple), C) endothelial cells (ECs, blue), D) T-cells (dark green), E) dendritic cells and macrophages (DCs, light green), and keratinocytes (KCs, yellow), melanocytes (Mel, brown); differentially expressed genes (DEGs) were calculated comparing 'PBMsec' skin biopsies to 'Medium' skin biopsies, using Wilcoxon rank sum test, including genes with average logarithmic fold change (avglogFC) of > 0.1 or < -0.1 and Bonferroni-adjusted p-value < 0.05 . For each cellgroup, top 50 DEGs according to lowest adjusted p-value are displayed, split by treatment. Dot size represents percent of cells expressing the respective gene, color correlates with average expression.

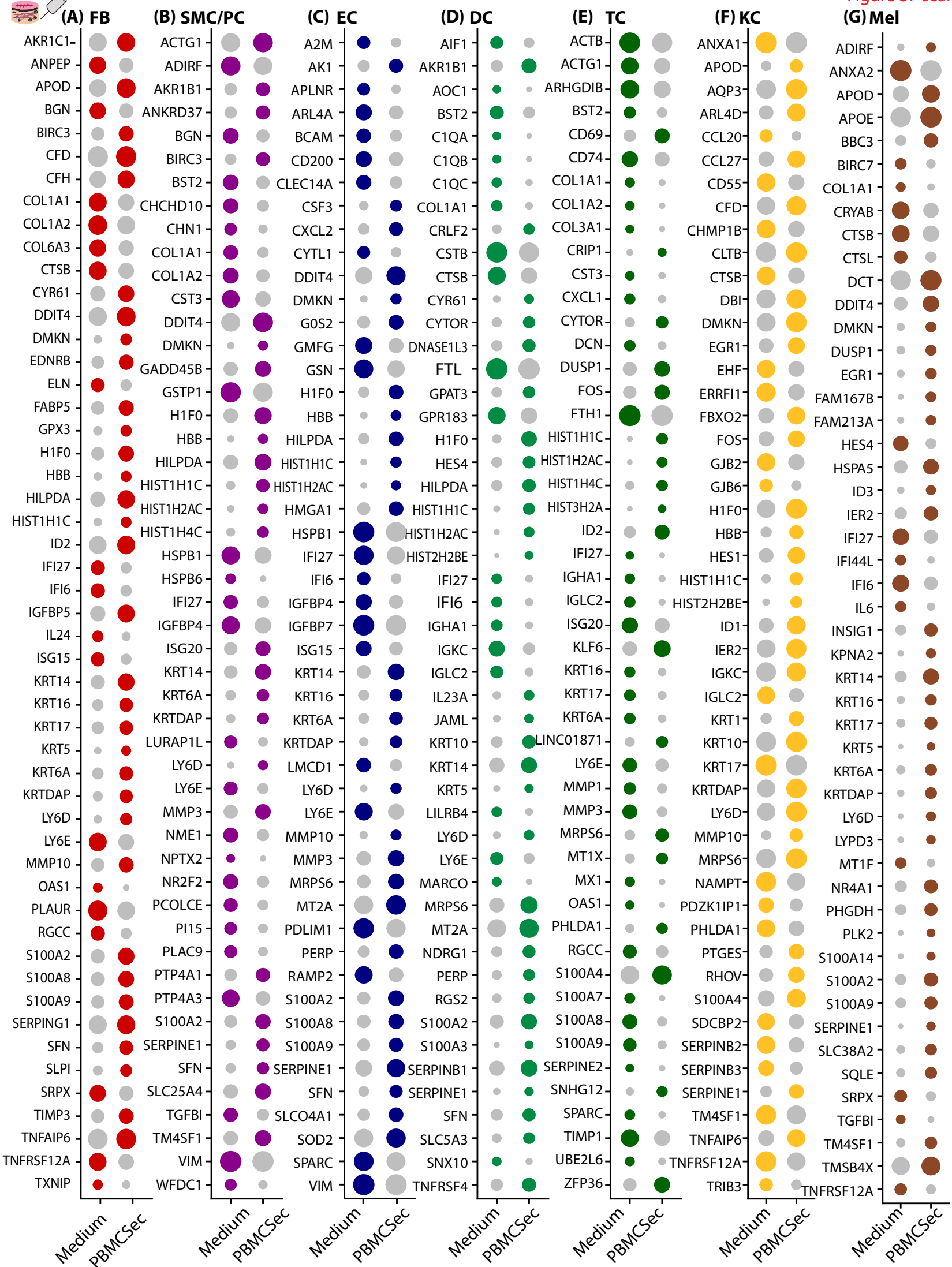


Figure S7: Top 50 regulated genes per cell group in human scar

In A) fibroblasts (FBs, red circles), B) smooth muscle cells and pericytes (SMC/PCs, purple), C) endothelial cells (ECs, blue), D) T-cells (dark green), E) dendritic cells and macrophages (DCs, light green), and keratinocytes (KCs, yellow), melanocytes (Mel, brown); differentially expressed genes (DEGs) were calculated comparing 'PBMsec' scar biopsies to 'Medium' scar biopsies, using Wilcoxon rank sum test, including genes with average logarithmic fold change (avglogFC) of > 0.1 or < -0.1 and Bonferroni-adjusted p-value < 0.05 . For each cellgroup, top 50 DEGs according to lowest adjusted p-value are displayed, split by treatment. Dot size represents percent of cells expressing the respective gene, color correlates with average expression.

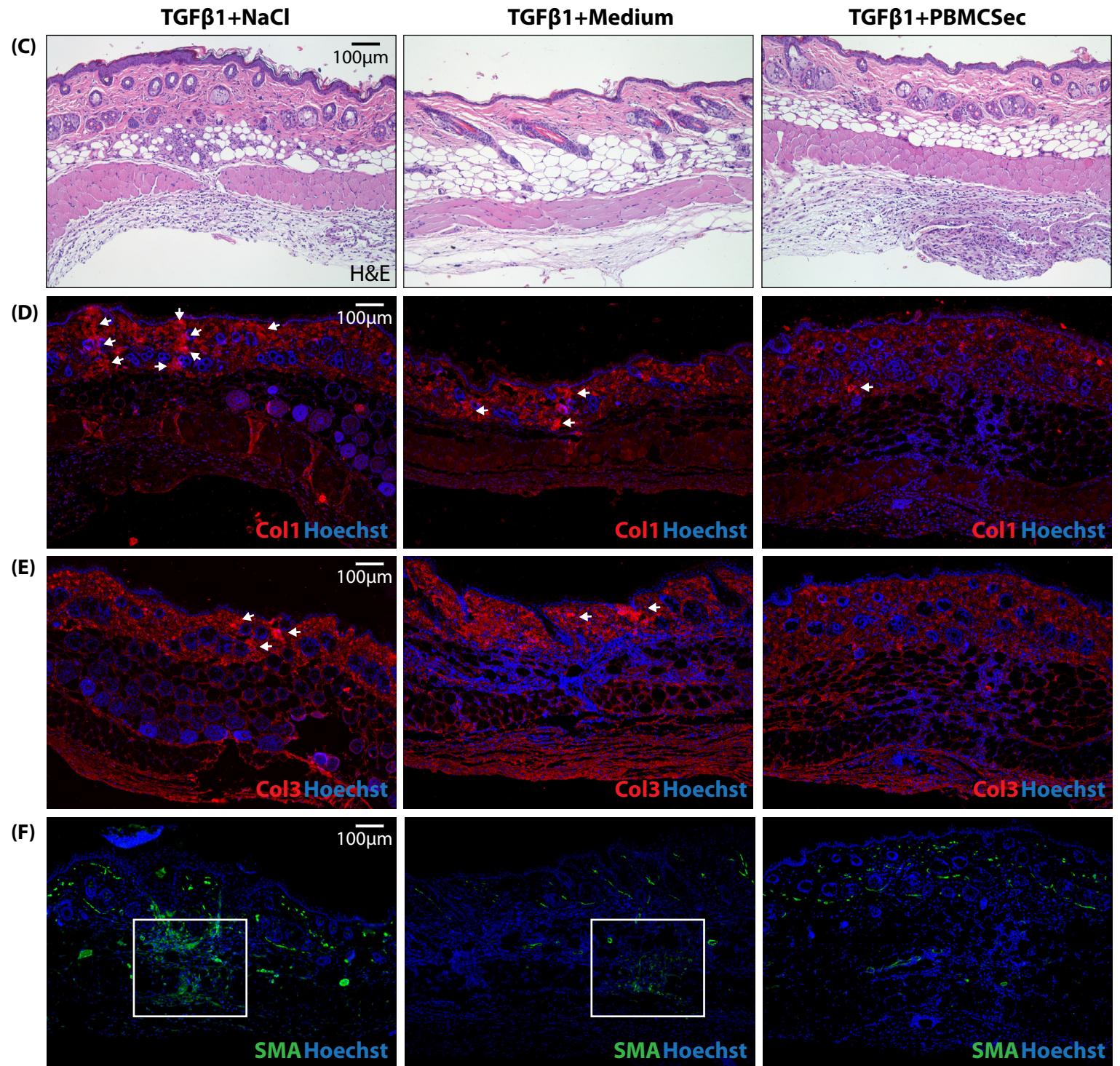
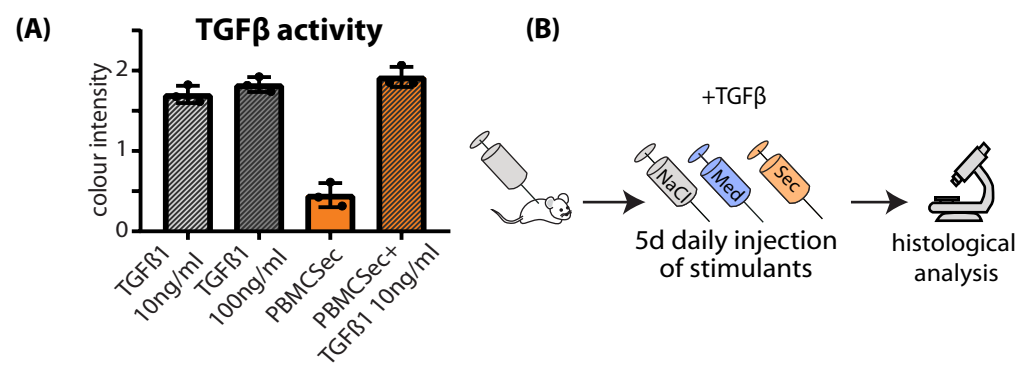


Figure S8: The interaction of TGF β and PBMCSec *in vivo*

A) In vitro TGF β -activity assay. HEK-cells colorimetrically detecting SMAD2/3 TGF β -activity were incubated with recombinant TGF β 1, with PBMCSec alone, and with TGF β 1 and PBMCSec combined. Color intensity correlates with TGF β 1-signaling activity. B) Workflow of mice intradermally injected with TGF β 1 and treatments. Mice were intradermally injected with 800ng TGF β 1 dissolved 100 μ l in NaCl 0,9%, Medium or PBMCSec on five consecutive days and sacrificed on the 6th day. C) H&E staining of resulting "scars" of the injected area. Immunofluorescence stainings of D) collagen 1, E) collagen 3, F) smooth muscle actin in TGF β 1-injected mouse skin. Arrows indicate areas of dense matrix deposition.

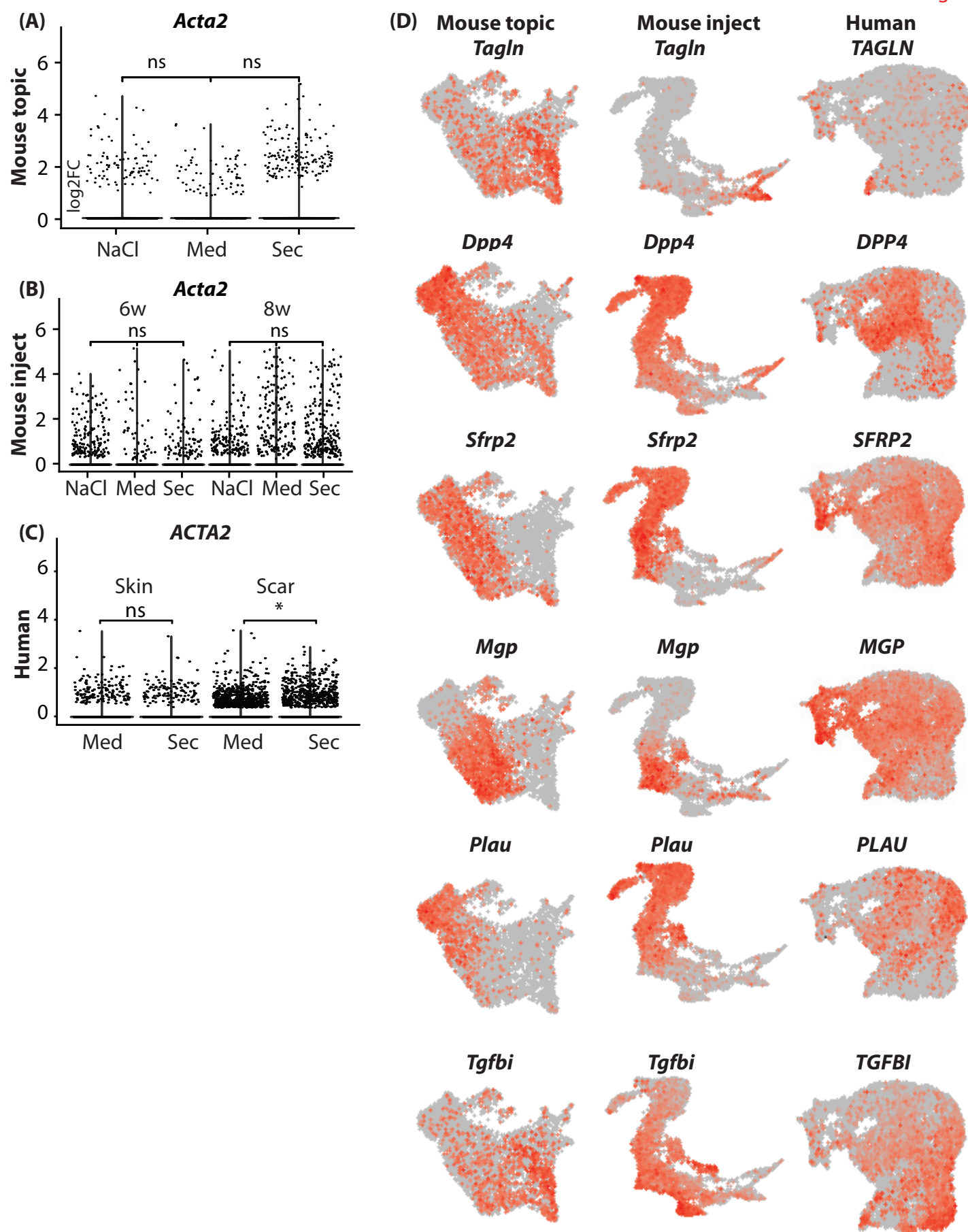


Figure S9: Subcluster analysis of FB populations

A-C) Violin plots of *Acta2/ACTA2* in mouse and human datasets, split by treatments. D) Feature plots of FB subcluster markers in FB subclusters of mouse and human datasets. *Tagln/TAGLN*, Transgelin; *Dpp4/DPP4*, dipeptidyl-peptidase 4; *Sfrp2/SFRP2*, Secreted Frizzled Related Protein 2; *Mgp/MGP*, Matrix Gla Protein; *Plau/PLAU*, urokinase; *Tgfbi/TGFBI*, Transforming Growth Factor Beta Induced. In violin plots, dots represent individual cells, y-axis represents log2 fold change of the normalized genes and log-transformed single-cell expression. Vertical lines in violin plots represent maximum expression, shape of each violin represents all results, and width of each violin represents frequency of cells at the respective expression level. In feature plots, normalized log expression of the respective gene is mapped onto the UMAP-plot. Color intensity indicates level of gene expressions. UMAP, uniform manifold approximation and projection. A two-sided Wilcoxon-signed rank test was used in R. NS $p > 0.05$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.