Supplemental data

Supplemental Table 1: Sequences of qPCR primers

Gene	Forward primer	Reverse primer
B2m	GTGACCCTGGTCTTTCTGGT	GTATGTTCGGCTTCCCATTC
Ppl	TTGAGACAGCAACCAGAAGC	TTCAGGGTCTGGATTTCCTC
Evpl	TGCTTCACCACCATGTTCAA	CGATCCTGTTGCAGCTTCTT
Kazn	GTGCAGCTGGTACAGAAGGA	TAGTTGCGGATGAAGTCTCG
Plec	GAACTTGCGACACAGGAGAA	AGTCTGCATCTCCTCCGACT
Col1a1	GTGGTGACAAGGGTGAGACA	GAGAACCAGGAGAACCAGGA
Col3a1	TACACCTGCTCCTGTGCTTC	CATTCCTCCCACTCCAGACT
Fn1	TGGTGGCCACTAAATACGAA	GGAGGGCTAACATTCTCCAG
Acta2	AGTCGCTGTCAGGAACCCTGAGA	ATTGTCGCACACCAGGGCTGTG
Vim	AAGAGATGGCTCGTCACCTT	GGGTGTCAACCAGAGGAAGT
Arg1	CTGGAACCCAGAGAGAGCAT	CTCCTCGAGGCTGTCCTTT
Cd206	TGATTACGAGCAGTGGAAGC	GTTCACCGTAAGCCCAATTT
Tnfa	TCGTAGCAAACCACCAAGTG	TTGTCTTTGAGATCCATGCC
Il1b	GCTTCCTTGTGCAAGTGTCT	GGTGGCATTTCACAGTTGAG
Il6	AGTCCGGAGAGGAGACTTCA	TTGCCATTGCACAACTCTTT
Cxcl1	CCGAAGTCATAGCCACACTC	GTGCCATCAGAGCAGTCTGT
Il1rn	GTCTTGTGCCAAGTCTGGAG	AGAGCGGATGAAGGTAAAGC
Il10	CCCAGAAATCAAGGAGCATT	TCACTCTTCACCTGCTCCAC
Rarres2	CAAGAGATCGGTGTGGACAG	GCTTAAATTCCAACCTCACAAA
Tgfb1	ACTGATACGCCTGAGTGGCT	CCCTGTATTCCGTCTCCTTG
Ctgf	GAGTGTGCACTGCCAAAGAT	GGCAAGTGCATTGGTATTTG
Cryab	AGGGAAGTGGCTGTTGAGAAG	GCCTCTTCGACCAGTTCTTCG
Itgb6	GCTGGTCTGCCTGTTTCTGC	TGAGCAGCTTTCTGCACCAC
Itgav		

Supplemental Table 2: List of antibodies

Target	Clone	Supplier
STAT3	124H6	Cell Signaling, France
Phospho-STAT3 (Tyr705)	D3A7	Cell Signaling, France
AKT	C67E7	Cell Signaling, France
Phospho-AKT (Ser473)	D9E	Cell Signaling, France
Anti-mouse CD16/CD32	2.4G2	BD Pharmingen, France
APC/Cy7 anti-mouse CD45	30-F11	BioLegend, France
PE anti-mouse Fcg RI/CD64	290322	R&D systems, France
F480-APC Cy7	BM8	BioLegend, France
CD11c-APC	HL3	BD Pharmingen, France
CD11b-Brilliant Violet 421	M1/70	BioLegend, France
CD11b-PE	M1/70	BioLegend, France
Ly6C-PE CY7	AL-21	BD Pharmingen, France
CD64-PerCP	290322	R&D systems, France
Ki67 Alexa Fluor 647	SolA15	eBioscience, France
Arg-1-PE	polyclonal	R&D systems, France
Biotinylated CD206	polyclonal	R&D systems, France
Ki67	M7249, clone TEC-3	Dako, Les Ulis, France
cCasp3	2305-PC-100	Trevigen, Gaithersburg, MD, USA
beta Tubulin	ab6046	Abcam, France

Supplemental figures & legends :

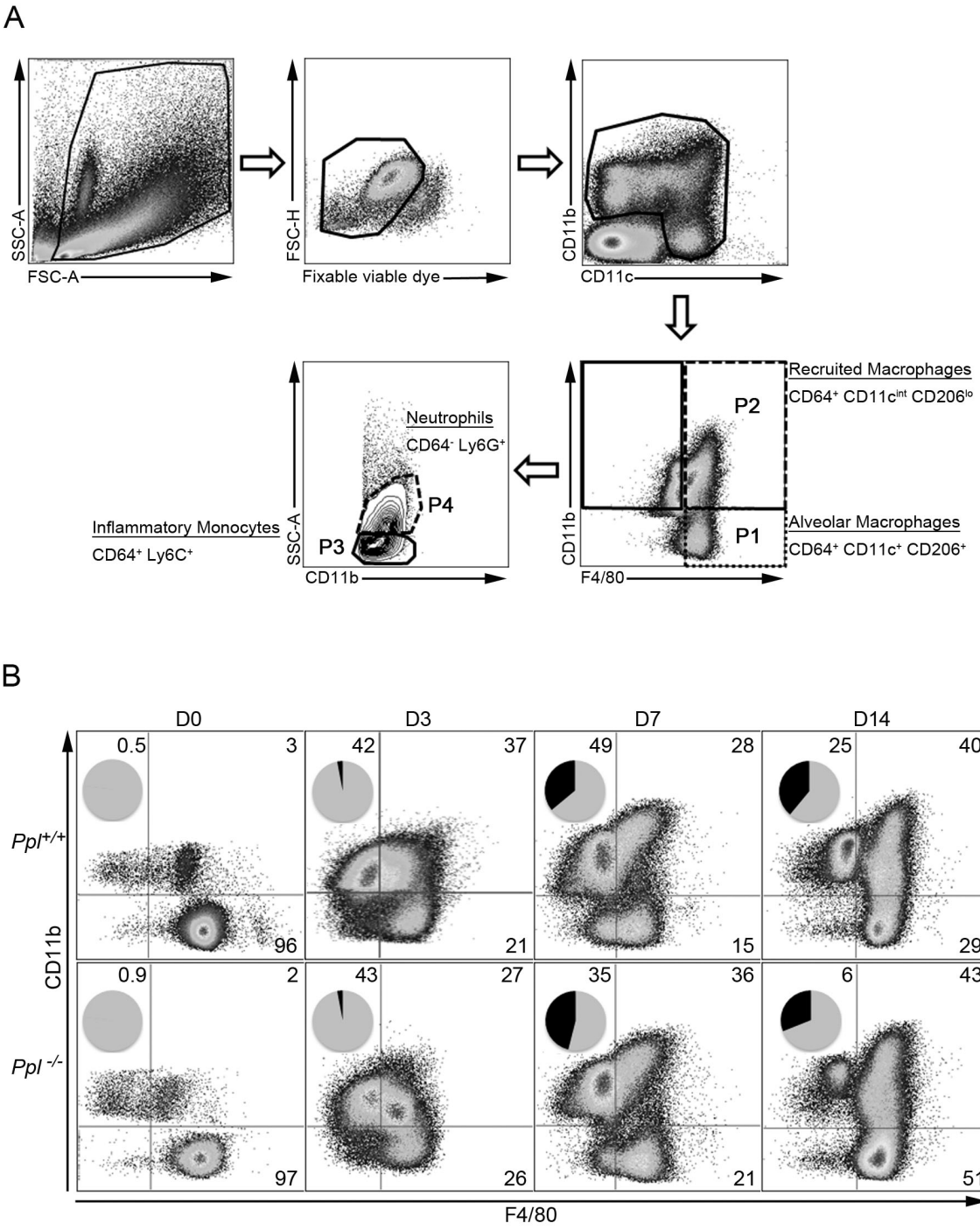

Figure S1 : FACS analysis.

(A) Monocytes/macrophages/Neutrophils subsets were identified by FACS analysis, after exclusion of cell debris using fixable viability dye, on CD64 gate, using F480 and CD11b markers. Simultaneous expression of Ly6C, CD11c was assessed within P1-P4 subsets. Inflammatory monocytes (P3) were defined by the expression of Ly6C and CD11b markers.

Recruited macrophages (P2) displayed Ly6Cint and CD11clow expression. Resident macrophages (P1) were identified as FSChigh CD11c+ Ly6C- and neutrophils (P4) were determined by CD64- Ly6G+ staining. (**B**) Representative flow cytometric profiles of BAL cells of *Ppl*+/+ and *Ppl*-/- mice after bleomycin exposure. Relative proportions (inserted table) of inflammatory monocyte and neutrophil subsets among BAL cells were inserted into FACS profiles for each indicated time point.

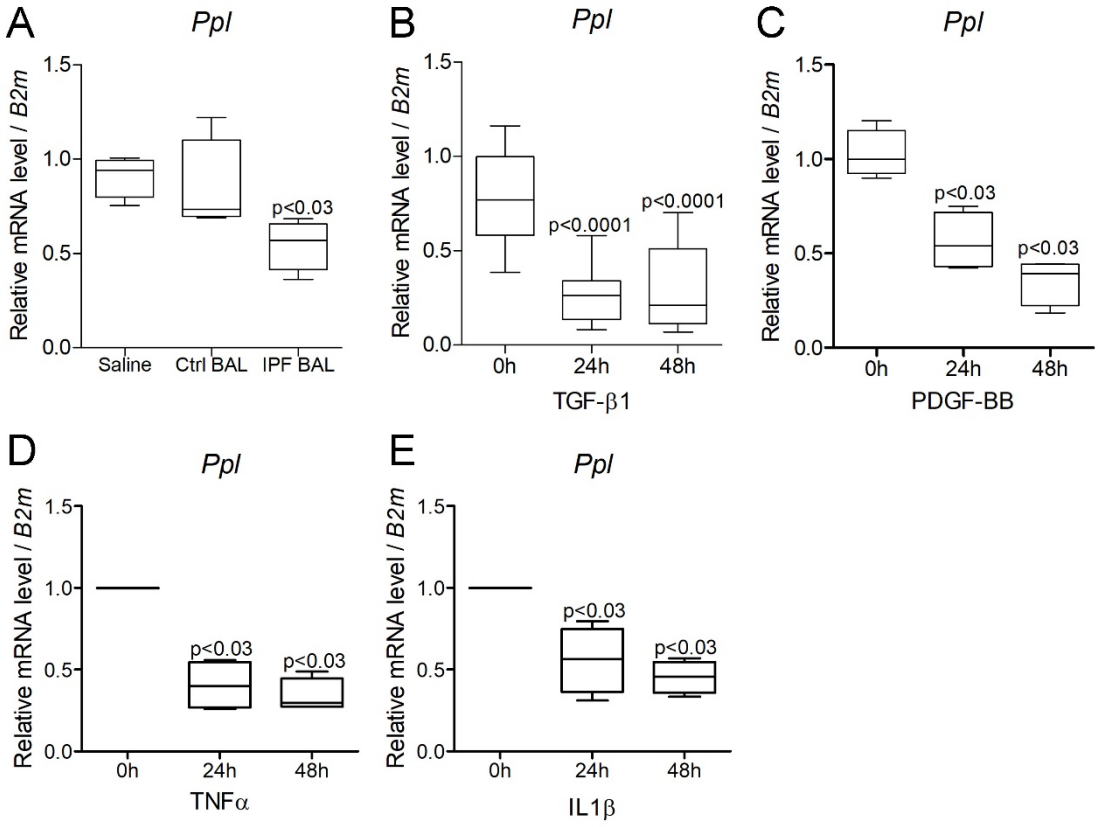

Figure S2 : Expression of PPL is decreased after lung injury

Ppl mRNAs were assessed by quantitative PCR and normalized to the β2-microglobulin (*B2m*) gene in (A) type 2 AECs exposed to either saline (0.9% NaCl), or BAL fluid from control (Ctrl) or (IPF) human patient for 24h, in type 2 AECs exposed to either hTGF-β1 (B), hPDGF-BB (C), hTNF-α (D), or hIL1β (E) for 24 and 48h. N = 5. Mann Whitney U test.

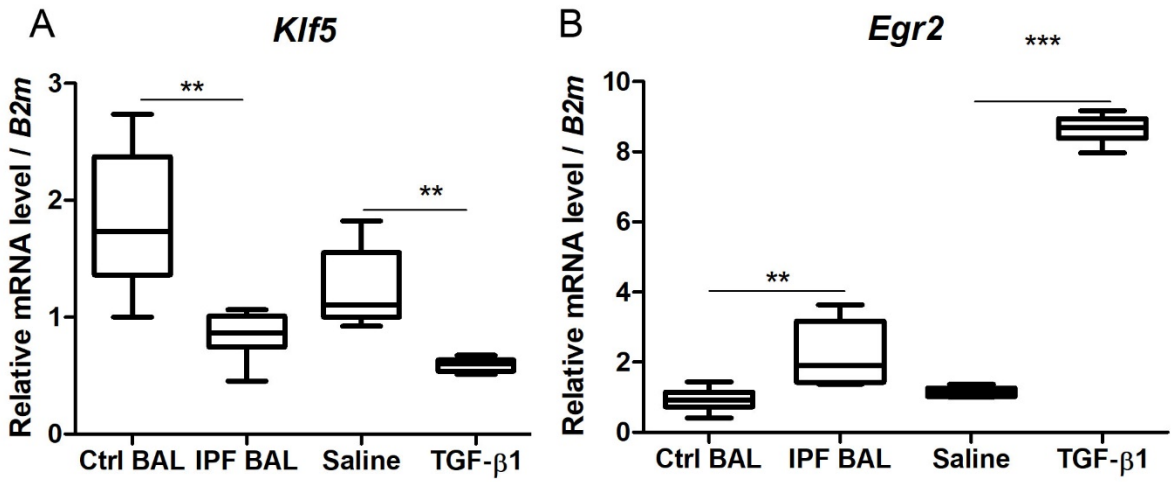

Figure S3 : *Klf5* and *Egr2* gene transcription in response BAL proteins

Primary type 2 AECs were exposed to either BAL fluid from control (Ctrl) or (IPF) human patient, or saline (0.9% NaCl), or hTGF-β1 for 24h and *Klf5* (A) and *Egr2* (B) mRNAs were assessed by quantitative PCR and normalized to the β2-microglobulin (*B2m*) gene. N = 5. ***p* < 0.01; ****p* < 0.001, Mann Whitney U test.

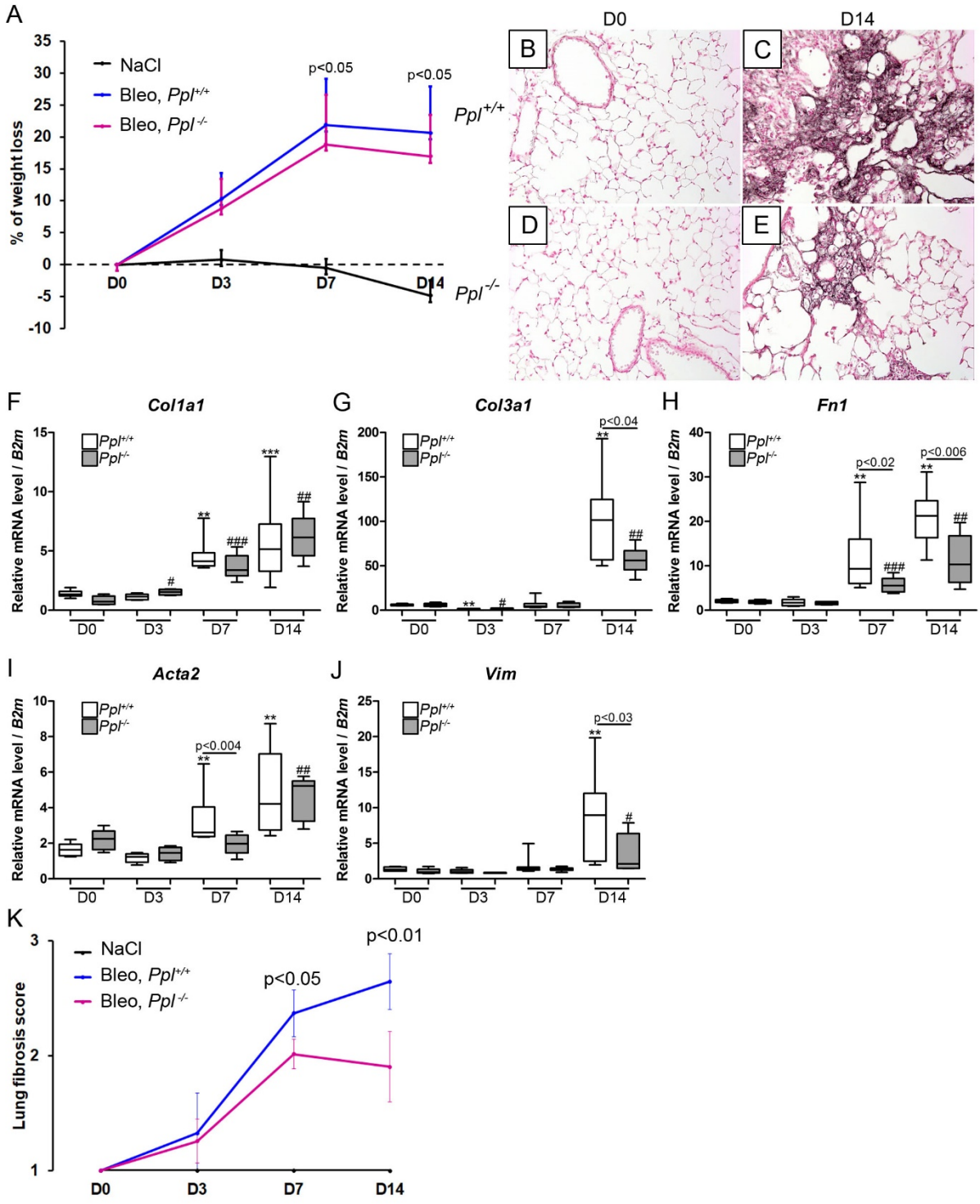

Figure S4 : Lung fibrosis in *Ppl*$^{-/-}$ mice.

(A) Percentage of body weight loss of *Ppl*$^{+/+}$ and *Ppl*$^{-/-}$ mice after bleomycin exposure. (B) Collagen deposition was assessed by immunostaining for type 3 collagen on lung sections of *Ppl*+/+ (a, b) and *Ppl*-/- mice (c, d) prepared at D0 and D14 after bleomycin exposure. Figure is representative of at least 6 individual mice at each time. Magnification x20. Collagen 3 deposition was less extensive in *Ppl*-/- mice compared to *Ppl*+/+ mice. *Col1a1* (C), *Col3a1*

(D), *Fn1* (E), *Acta2* (F), and *Vim* (G) mRNAs were assessed by quantitative PCR in whole lung homogenate from *Ppl*+/+ and *Ppl*-/- mice at indicated time points after bleomycin instillation and normalized to *B2m* mRNA. N = 5-8. (H) Lung fibrosis score of $Ppl^{+/+}$ and $Ppl^{-/-}$ mice after bleomycin exposure.

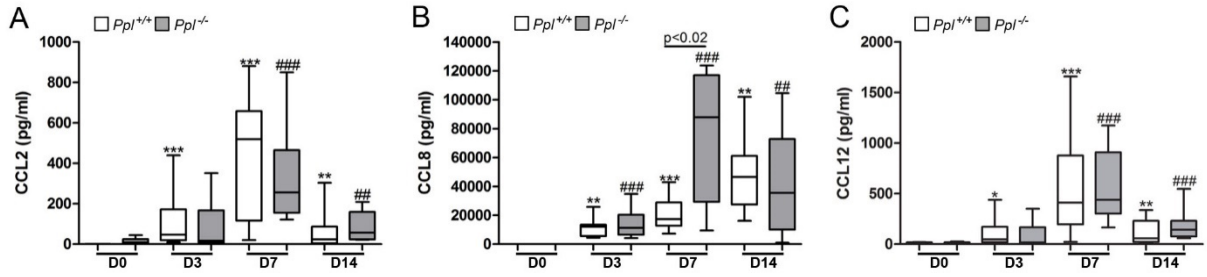

Figure S5 : Proinflammatory chemokines in BAL.

CCL2 (**A**), CCL8 (**B**) and CCL12 (**C**) concentration was measured by ELISA in BAL fluid from *Ppl*+/+ and *Ppl*-/- mice in normal condition and after bleomycin treatment at indicated time points. N = 7-9 mice per group. *$p < 0.05$ vs. (D0, *Ppl*+/+); **$p < 0.01$ vs. (D0, *Ppl*+/+); ***$p < 0.001$ vs. (D0, *Ppl*+/+); # *p<0.05* vs. (D0, *Ppl*-/-); ## *p<0.01* vs. (D0, *Ppl*-/-). Mann Whitney U test.

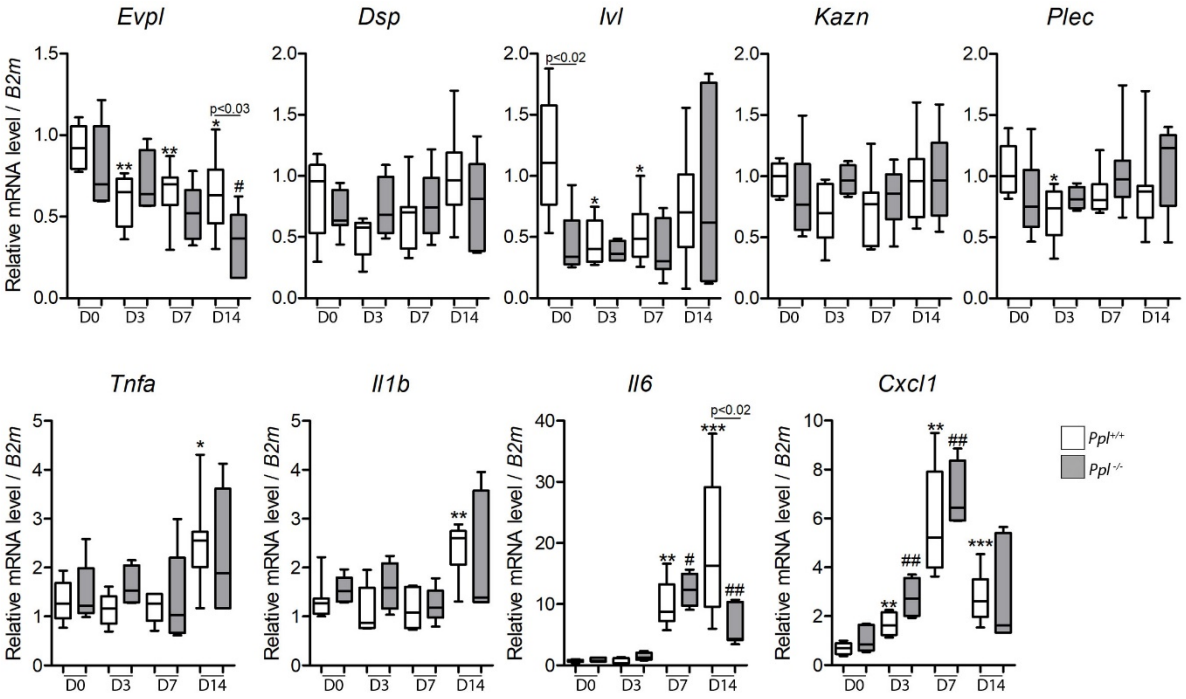

Figure S6 : Transcriptional expression of desmosome associated genes an pro-inflammatory genes.

Quantitative RT-PCRs for *Evp, Dsp*, *Ivl, Kazn, Plec, Tnfa, Il1b, Il6 and Cxcl1* mRNAs were performed on $Ppl^{+/+}$ and $Ppl^{-/-}$ lung homogenates after bleomycin instillation and normalized

to *B2m* mRNA. Results are expressed as means ± SE of 5 animals per group. **p* < 0.05 vs. (D0, *Ppl*$^{+/+}$); ***p* < 0.01 vs. (D0, *Ppl*$^{+/+}$); ****p* < 0.001 vs. (D0, *Ppl*$^{+/+}$); # *p<0.05* vs. (D0, *Ppl*$^{-/-}$); ## *p<0.01* vs. (D0, *Ppl*$^{-/-}$) Mann Whitney U test.