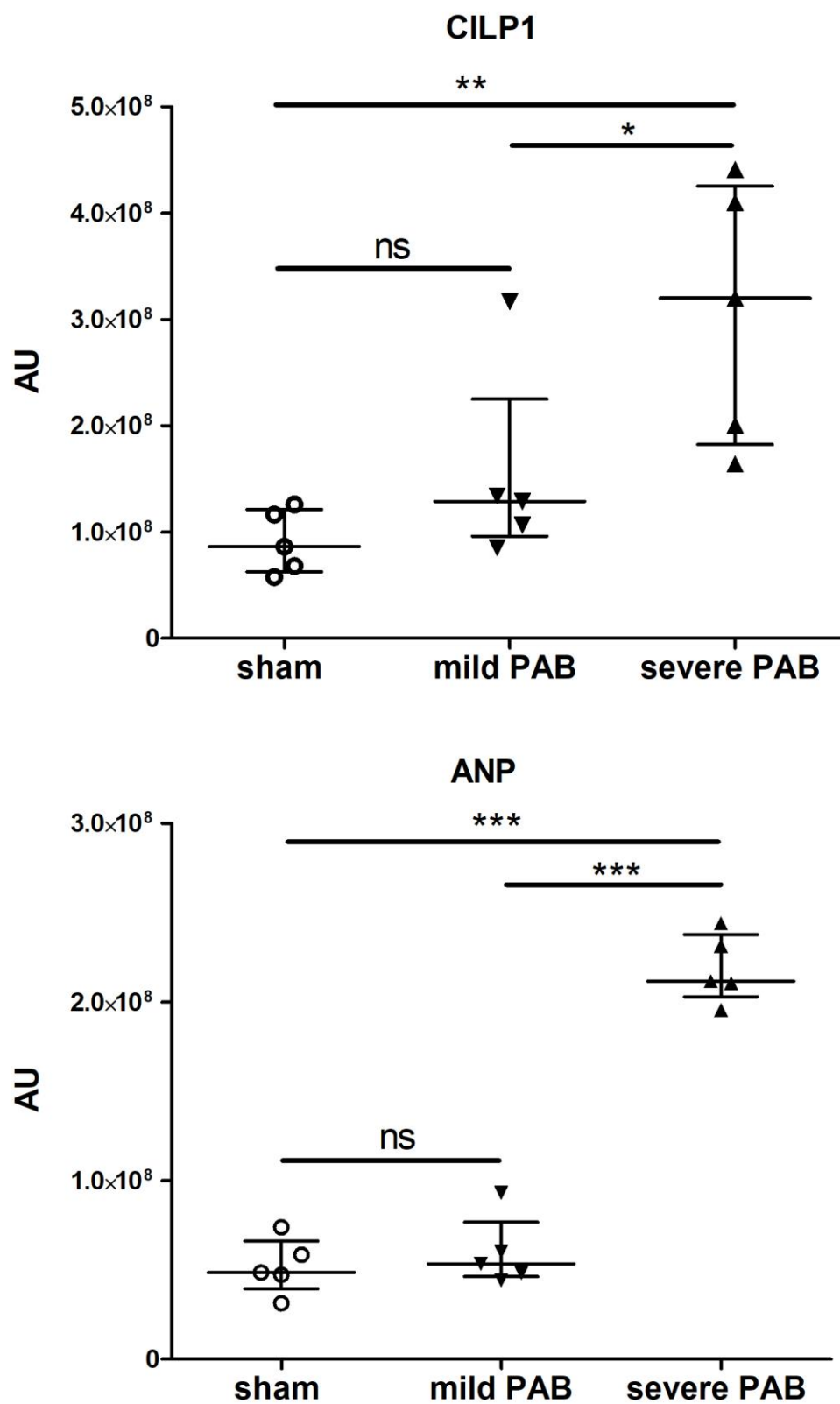


CILP1 as a biomarker for right ventricular maladaptation in pulmonary hypertension

Supplementary material

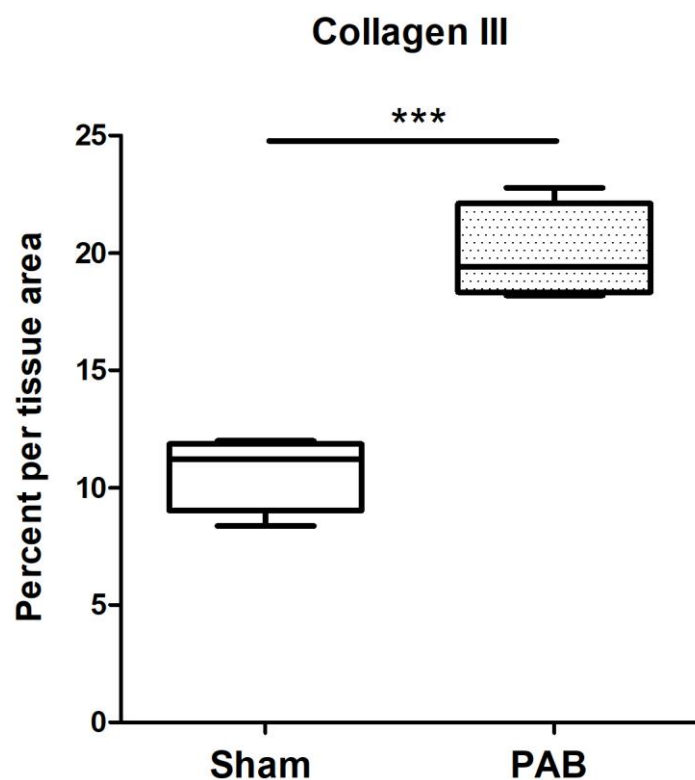
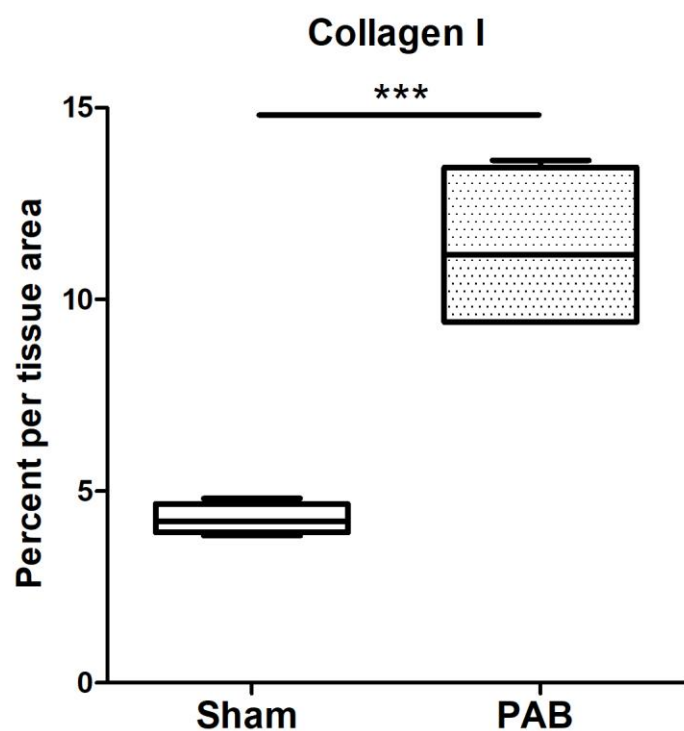
Suppl. Figure S1: Box plots comparing (A) CILP1 and (B) ANP protein concentrations in murine RV one week after sham, mild PAB, and severe PAB

Data were obtained from quantitative western blot band intensity analysis



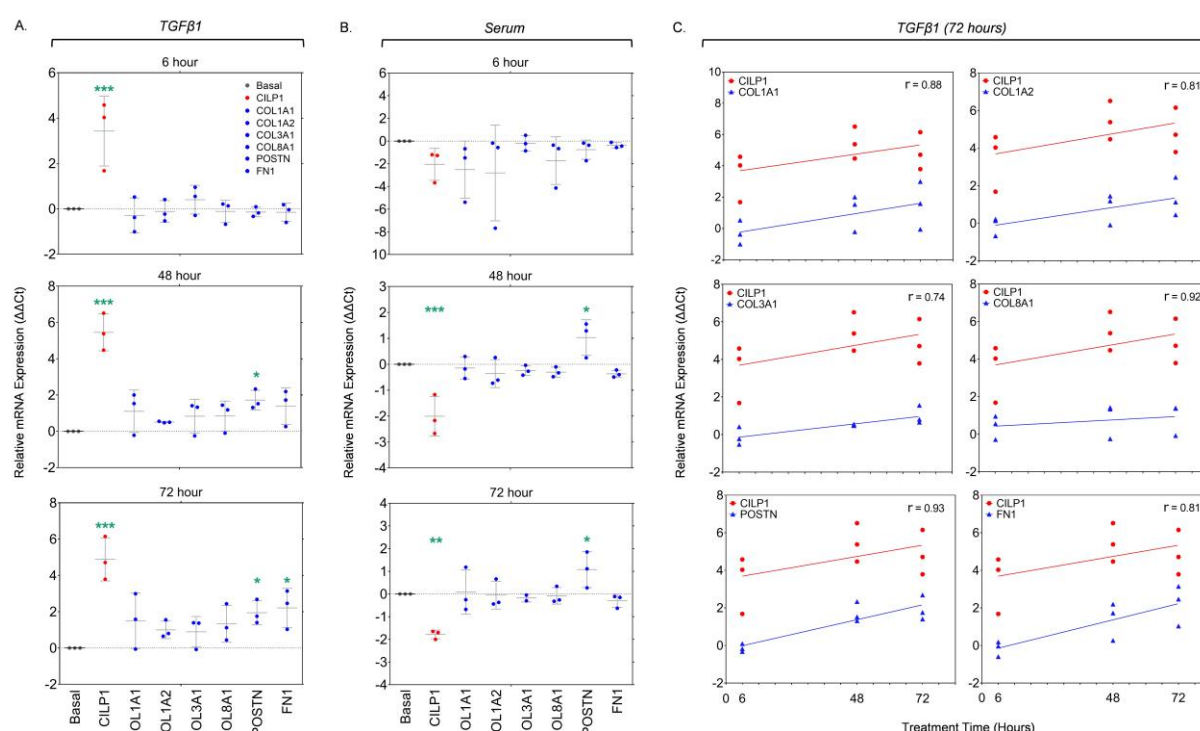
Suppl. Figure S2: Box plots comparing the amount of collagen I (A) and III (B) in murine RV one week after sham and severe PAB.

Data were obtained from quantitative immunofluorescence measurements are expressed as percent of the signal per tissue area. Boxes represent median with IQR. (n=4 in each group, ***p<0.001)



Suppl. Figure S3: Analysis of CILP1, COL1A1, COL1A2, COL3A1, COL8A1, POSTN, and FN1 expression in human cardiac fibroblasts under stimulation with (A) transforming growth factor beta 1 (TGF β 1, 5 ng/ml), or (B) fetal bovine serum for 6, 48 and 72 hours; (C) Correlation analysis between the gene expression levels of CILP1 and COL1A1, COL1A2, COL3A1, COL8A1, POSTN, and FN1 under TGF β 1 at 72 hours.

The gene expression levels of CILP1, COL1A1, COL1A2, COL3A1, COL8A1, POSTN, and FN1 were measured by real-time polymerase chain reaction (PCR). The data was normalized to the housekeeping gene hypoxanthine-guanine phosphoribosyltransferase (HPRT1) and untreated control (basal medium without addition of serum or TGF β 1). The $\Delta\Delta C_t$ values are expressed as mean (SD), (n=3, *p < 0.05 versus basal medium)



Suppl. Table S1: Clinical characteristics of IPAH and CTEPH patients

	Adaptive CTEPH n=22	Maladaptive CTEPH n=13	Adaptive IPAH n=25	Maladaptive IPAH n=37
Female sex, n (%)	10 (45)	4 (31)	16 (64)	23 (62)
Age, y, median (IQR)	67 (64-72)	58 (53-63)	60 (50-69)	60 (41-71)
BMI, kg/m ² , median (IQR)	24 (24-29)	26 (26-28)	29 (26-32)	26 (22-30)
CAD, n (%)	4 (18)	3 (23)	4 (16)	10 (28)
NYHA \geq III, n (%)	14 (74)	6 (55)	7 (58)	15 (71)
Diabetes, n (%)	5 (23)	2 (15)	7 (28)	10 (28)
Right Heart Catheterization				
PASP, mmHg, median (IQR)	56 (46-65)	88 (70-93)	64 (52-78)	88 (77-105)
PAPmean, mmHg, median (IQR)	36 (29-41)	55 (44-58)	40 (33-49)	55 (48-65)
Cardiac index, L/min/m ² , median (IQR)	2,92 (2,76-3,30)	1,86 (1,60-1,95)	3,13 (2,80-3,33)	1,70 (1,47-2,02)
PAWPmean, mmHg, median (IQR)	8 (8-12)	9 (8-11)	10 (7-12)	10 (7-12)
RAP, mmHg, median (IQR)	5 (5-7)	11 (6-16)	5 (4-11)	10 (8-13)
Echocardiography				
TAPSE, mm, median (IQR)	23 (21-26)	16 (11-16)	22 (21-25)	14 (12-16)
LVEF, median (IQR)	62 (59-67)	60 (58-63)	65 (60-71)	65 (60-70)
RVD, mm, median (IQR)	39,5 (33-45)	49 (47-57)	40 (37-44)	50 (47-52)
IVSd, mm, median (IQR)	10 (9-11)	10 (9-12)	9 (9-11)	10 (9-11)
LVPWd, mm, median (IQR)	9,5 (9-10)	10 (9-10)	9 (6-10)	10 (10-11)
TAPSE/PASP	0,40 (0,34-0,51)	0,16 (0,14-0,21)	0,35 (0,27-0,49)	0,16 (0,13-0,21)
CILP1, pg/ml, median (IQR)	3426 (2872-3812)	5643 (5053-6008)	4092 (2720-4687)	5764 (4375-6341)
NT-pro-BNP, pg/ml, median (IQR)	193 (95-367)	1138 (999-2197)	70 (39-133)	573 (209-1488)

Abbreviations: BMI body mass index; CAD, coronary artery disease; NYHA, New York Heart Association; PASP pulmonary arterial systolic pressure; PAPmean, mean pulmonary artery pressure; PAWPmean, mean pulmonary artery wedge pressure; RAP right atrial pressure; TAPSE, tricuspid annular plane systolic excursion; LVEF, left ventricular ejection fraction; RVD, right ventricular diameter; IVSd, diastolic interventricular septum thickness, LVPWd, diastolic left ventricular posterior wall thickness

Suppl. Table S2: Multivariable analysis of parameters as predictors of high serum CILP concentration

Variable	p-value	Odds Ratio	95 CI
PAPmean	0.39	0.98	0.92-1.03
RVD	0.13	1.06	0.98-1.13
TAPSE/PASP	0.01	0.08	0.01-0.52

Abbreviations: PAPmean, mean pulmonary artery pressure; RVD, right ventricular diameter; TAPSE, tricuspid annular plane systolic excursion; PASP pulmonary arterial systolic pressure