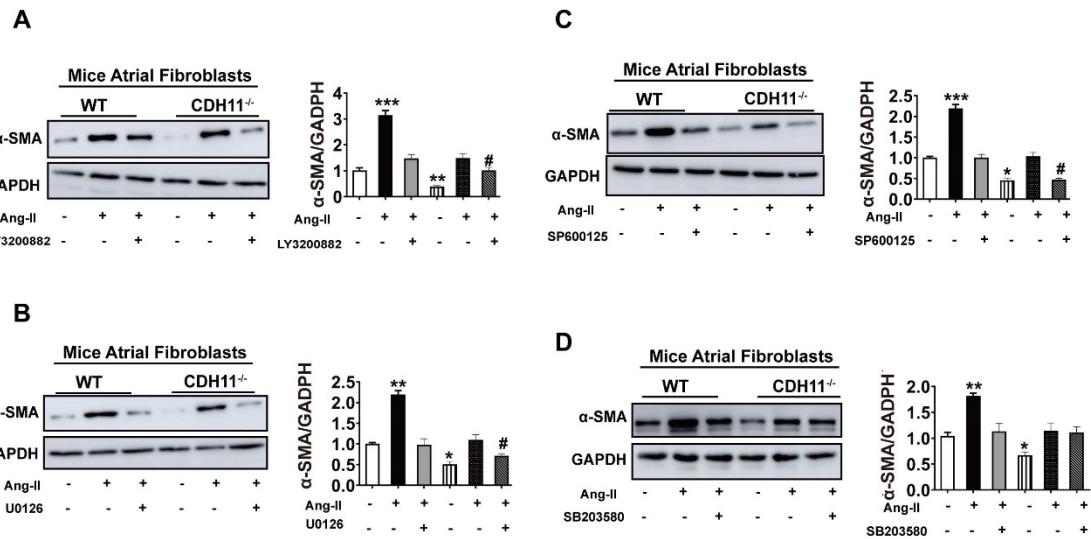
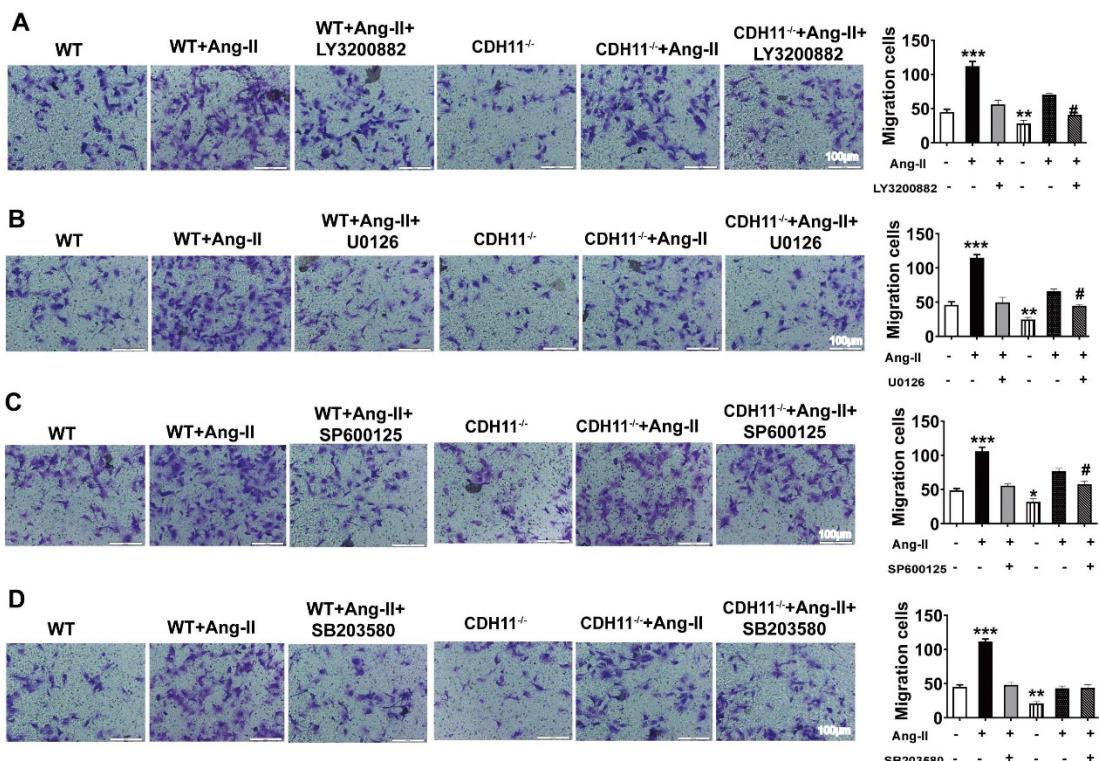


Supplementary Figure 1



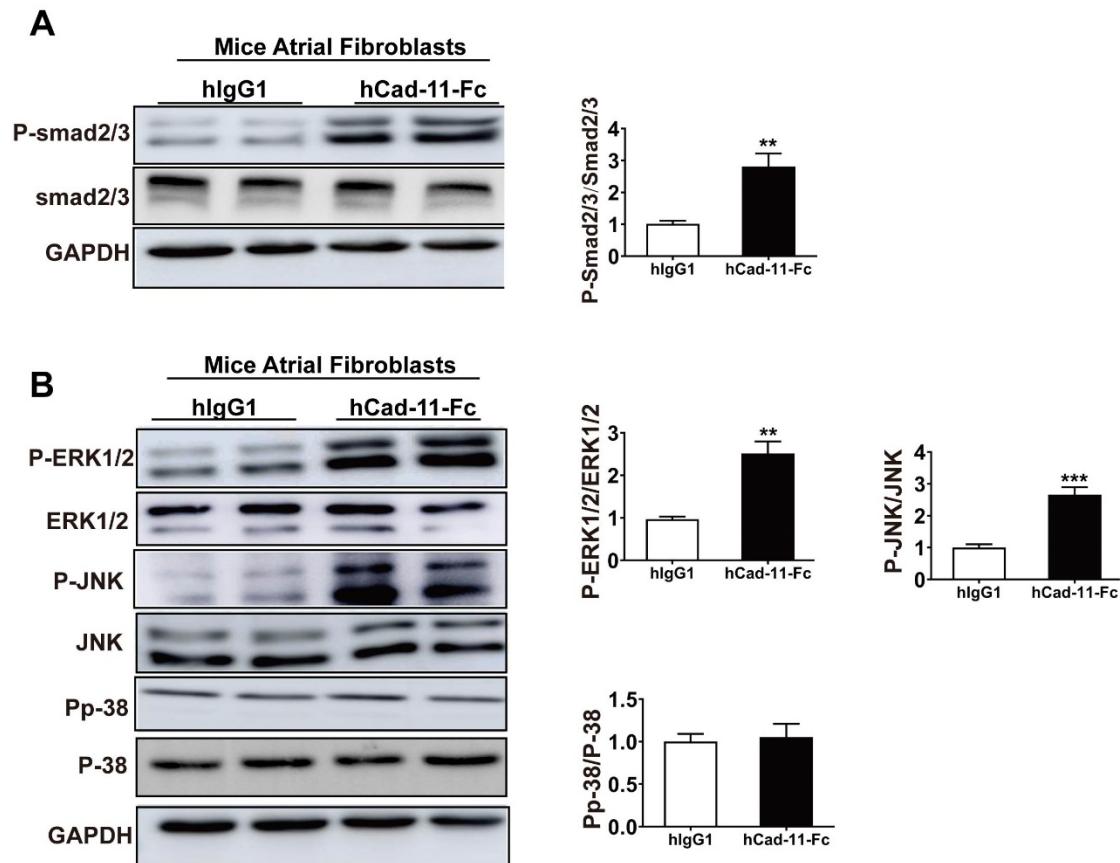
Supplementary Figure 1. Loss of CDH11 attenuated Ang-II-induced differentiation of AFs in the presence of Smad2/3 and MAPK signalling inhibitors. AF cells isolated from CDH^{-/-} and WT mice were cultured and pre-treated with signalling inhibitors as indicated, followed by treatment of Ang-II (1 μ M, 24h) and harvesting for *Western* blotting analysis. **A~D:** Representative *Western* blotting image and summaries of the protein levels of the differentiation marker α -SMA protein in AFs treated with Smad2/3 inhibitor LY3200882 (**A**); or ERK pathway inhibitor U0126 (**B**); or JNK inhibitor SP600125 (**C**); or P38 inhibitor SB203580 (**D**) followed with or without Ang-II stimulation. Data are presented as mean \pm SD. *: $p<0.05$, **: $p<0.01$, ***: $p<0.001$ vs Ctl. #: $p<0.05$.

Supplementary Figure 2



Supplementary Figure 2. Loss of CDH11 attenuated Ang-II-induced atrial fibroblast cell migration in the presence of Smad2/3 and MAPK signalling inhibitors. AF cells isolated from CDH^{-/-} and WT mice were cultured in Transwell and pre-treated with signalling inhibitors as indicated, followed by treatment of Ang-II (1 μ M, 24h). Migrated cell numbers were counted. **A~D:** Representative cell image and summaries of the cell numbers of the migrated cells in AFs pretreated with Smad2/3 inhibitor LY3200882 (**A**); or ERK inhibitor U0126 (**B**); or JNK inhibitor SP600125 (**C**); or P38 inhibitor SB203580 (**D**) followed by Ang-II or vehicle control stimulation. Data are presented as mean \pm SE. *: $p<0.05$, **: $p<0.01$, ***: $p<0.001$ vs Ctl. #: $p<0.05$.

Supplementary Figure 3



Supplementary Figure 3. CDH11-Fc activates the downstream Smad2/3, ERK1/2 and JNK pathway in AFs. AFs were isolated from WT mice, cultured and serum-starved for 24h, followed by treatment of hCDH11-Fc (10 μ g/ml; 24h). **A** and **B**: Illustrated are representative Western blotting images and summaries of hCDH11-Fc-mediated changes in phosphorylation of Smad2/3 (A), ERK1/2 and JNK (B). Data are presented as mean \pm SD. *: $p<0.05$, **: $p<0.01$ vs hIgG1.

Supplementary Table 1. Clinical characteristics of patients with atrial fibrillation or SR undergoing coronary artery bypass graft surgery.

	SR (n=8)	atrial fibrillation (n=11)
Ages (years old)	57.31±2.18	58.24±1.61
Female n (%)	2 (25%)	4(36%)
Echocardiographic parameters		
LA diameter (cm)	4.07±0.36	4.89±0.76
LA volume (ml)	59.52 ± 13.4	67.43 ± 10.56
LVEF (%)	64.63 ± 3.67	67.52± 3.57
FS (%)	42.23 ± 2.21	41.05 ± 3.43
Diseases		
HF (%)	12.5%	9.1%
Hypertension (%)	12.5%	36.7%
Mitral valve stenosis (%)	50%	45.4%
Mitral insufficiency (%)	37.5%	54.5%
Diabetes (%)	0%	18.2%
Medical therapy prior to the surgery		
Dabigatran etexilate n (%)	0 (0.0%)	6(54.5%)
Warfain n(%)	0 (0.0%)	3(27.3%)
Statin n (%)	3 (37.5%)	6 (54.5%)
β-blockers n (%)	5 (62.5%)	4 (36.7%)
ACE1/ARB n (%)	1 (12.5%)	4 (36.7%)
Aldosterone antagonist n (%)	0 (0.0%)	2(18.2%)
Calcium antagonist n (%)	0 (0.0%)	1 (9.1%)
Amiodarone n (%)	0 (0.0%)	4 (36.7%)

SR: sinus rhythm; LA: left atrium; LVEF: left ventricular ejection fraction; FS: fractional shortening; HF: heart failure; ACEI: angiotensin-converting enzyme inhibitor; and ARB: angiotensin receptor blocker.

Supplementary Table 2. Primers and Probes for genes analyzed by qRT-PCR.

Gene	Forward Primer	Reverse Primer	Probe
CDH11(H)	5'-GGCCCCAAGTTACATCCACG-3'	5'-CCTTATCGGGCTGTTGGCAG-3'	5-FAM'- AATGCAGCTGCTGGCACCGTGTTG-3'- BHQ1'
GAPDH(H)	5'-TCATCAGCAATGCCCTCTGC-3'	5'-CAGTCTCTGGGTGGCAGTG-3'	5-FAM'- ACCAACTGCTTAGCACCCCTGGCCA-3'- BHQ1'
CDH11(M)	5'-TCTCTCAGGTGAAGGAGCGG-3'	5'-GCTCCAGTGGCTGTTGGT-3'	5-FAM'- ACACACTGATGGCTAGGCGGTGGACA- 3-BHQ1'
Fgf10(M)	5'-ATGTCCGCTGGAGAAGGCT-3'	5'-TGGCTTGACGGCAACAACT-3'	5-FAM'- ACGGCAAGGTAGCGGGACCAAGAA-3'- BHQ1'
MMP9(M)	5'-CTATCGGCCTGCACCACAG-3'	5'-CACAGGGTTGCCTCTCCG-3'	5-FAM'- AACGACGGCACGCCCTGGTAGCA-3'- BHQ1'
BMP9(M)	5-CAGTGTCCCTCCAGGTTCCA-3'	5'-GCATGGTCTCCTGCTCATGG-3'	5-FAM'- ACCGCAGCAATGGGACCAAGGAGACCA- 3-BHQ1'
FN1(M)	5'-CGGCTACATCATCCGCCATC-3'	5'-CTGACAAACGTACTCGGTGCC-3'	5-FAM'- ACGCCGAGCATTCTGTCGGAAGACCCA- 3-BHQ1'
ACTA2(M)	5'-TCATGCCATCATCGCTCTGG-3'	5'-ATCTCACGCTGGCAGTAGT-3'	5-FAM'- ACTTGGCTGGCCGAGATCTCACCGACT- 3-BHQ1'
CTGF(M)	5'-GGGCATCTCCACCCGAGTTA-3'	5'-TCCGGATGCACCTTTGCC-3'	5-FAM'- AAGCAGAGCCGCCCTGCATGGTCA-3-

			BHQ1'
COL1A1(M)	5'-CTGCTCCTCCAGGGATCCAA-3'	5'-CCAAGTTCCGGTGTGACTCG-3'	5-FAM'- TACAGCACCCCTTGAGGGCTGCA-3- BHQ1'
COL3A1(M)	5'-CAGTGATGGGCAACCTGGTC-3'	5'-CTGCAGGTCCAACTTCACCC-3'	5-FAM'- ACTGCAGGATTCCCTGGATCCCCCTGGT- 3-BHQ1'
GAPDH(M)	5'-TTGGCATTGTGGAAGGGCTC-3'	5'-ATCACGCCACAGCTTCCAG-3'	5-FAM'- ACCACAGTCCATGCCCATCACTGCCACC- 3-BHQ1'

H: human; M: mouse.