**Supplementary materials**

**Supplementary Table 1.** Baseline characteristics of study patients.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **SR**(*n* = 10) | **pAF**(*n* = 10) | **cAF**(*n* = 10) |
| ***Demographics*** |
| Men, *n* (%) | 8 (80) | 6 (60) | 6 (60) |
| Age, years | 50 ± 15 | 52 ± 12 | 51 ± 11 |
| Body mass index, kg/m² | 24 ± 3 | 24 ± 5 | 24 ± 5 |
| ***Medical history*** |
| CAD, *n* (%) | 0 (0) | 5 (50)\* | 0 (0) |
| AVD, *n* (%) | 2 (20) | 4 (40) | 0 (0) |
| MVD, *n* (%) | 9 (90) | 8 (80) | 8 (80) |
| CAD + AVD, *n* (%) | 0 (0) | 3 (30) | 0 (0) |
| ICM, *n* (%) | 4 (40) | 2 (20) | 3 (30) |
| DCM, *n* (%) | 6 (60) | 8 (80) | 4 (40) |
| PPCM, *n* (%) | 0 (0) | 0 (0) | 1 (10) |
| Amyloidosis, *n* (%) | 0 (0) | 0 (0) | 2 (20) |
| Hypertension, *n* (%) | 4 (40) | 5 (50) | 3 (30) |
| Diabetes, *n* (%) | 4 (40) | 5 (50) | 2 (20) |
| Hyperlipidemia, *n* (%) | 3 (30) | 4 (40) | 4 (40) |
| ***Echocardiography*** |
| LA size (mm) | 47 ± 3 | 51 ± 7 | 49 ± 9 |
| LVEF (%) | 19 ± 6 | 21 ± 9 | 17 ± 9 |
| ***Medication*** |
| Amiodarone, *n* (%) | 4 (40) | 3 (30) | 3 (30) |
| Ivabradine, *n* (%) | 3 (30) | 0 (0) | 2 (20) |
| Digitalis, *n* (%) | 3 (30) | 5 (50) | 7 (70) |
| ACE inhibitors, *n* (%) | 8 (80) | 6 (60) | 7 (70) |
| AT1 blockers, *n* (%) | 1 (10) | 2 (20) | 1 (10) |
| Βeta-blockers, *n* (%) | 9 (90) | 10 (100) | 8 (80) |
| Diuretics, *n* (%) | 9 (90) | 10 (100) | 10 (100) |
| Nitrates, *n* (%) | 0 (0) | 0 (0) | 0 (0) |
| Lipid-lowering drugs, *n* (%) | 6 (60) | 4 (40) | 4 (40) |
| OAC,*n* (%) | 8 (80) | 7 (70) | 6 (60) |

Please note that patient characteristics have been published previously.1-4 ACE indicates angiotensin converting enzyme; AT, angiotensin receptor; AVD, aortic valve disease; CAD, coronary artery disease (non-obstructive concomitant CAD, not explaining severe LVEF reduction); cAF, chronic atrial fibrillation; DCM, dilated cardiomyopathy; ICM, ischemic cardiomyopathy (including severe CAD); LA, left atrial; LVEF, left ventricular ejection fraction; MVD, mitral valve disease; OAC, oral anticoagulation; pAF, paroxysmal atrial fibrillation; PPCM, peripartum cardiomyopathy; SR, sinus rhythm. Statistical comparisons between pAF / cAF *versus* SR groups were performed using ANOVA followed by Bonferroni correction for continuous variables and chi-square tests for categorical variables; \**P*<0.05 *versus* SR.

**Supplementary Table 2.** Short Tandem Repeat (STR) profiling of HL-1 cells.

|  |  |  |
| --- | --- | --- |
| **Locus** | **HL-1 cells used in this study, obtained from Dr. Claycomb (ID: musa0873)** | **HL-1 cells commercially available at Sigma-Aldrich (ID: musa0874)** |
| 18-3 | 16 |  | 16 |  |
| 4-2 | 20.3 |  | 20.3 |  |
| 6-7 | 12 | 17 | 12 | 17 |
| 19-2 | 13 |  | 13 |  |
| 1-2 | 19 |  | 19 |  |
| 7-1 | 26.2 |  | 26.2 |  |
| 1-1 | 17 |  | 17 |  |
| 3-2 | 14 |  | 14 |  |
| 8-1 | 16 |  | 16 |  |
| 2-1 | 16 |  | 16 |  |
| 15-3 | 21.3 | 22.3 | 21.3 | 22.3 |
| 6-4 | 18 |  | 18 |  |
| 11-2 | 16 |  | 16 |  |
| 17-2 | 15 | 16 | 15 |  |
| 12-1 | 17 |  | 17 |  |
| 5-5 | 17 | 18 | 17 | 18 |
| X-1 | 27 | 28 | 28 |  |
| 13-1 | 17 |  | 17 |  |
| Number of shared alleles between samples: | 21 |
| Total number of alleles in HL-1 cells used in this study: | 23 |
| Total number of alleles in HL-1 cells obtained from Sigma-Aldrich: | 21 |
| Percent match1 between samples: | 91 |

1Cell lines with ≥80% match are considered to be related.

**Supplementary Table 3.** TaqMan primers used for real-time quantitative polymerase chain reactions.

|  |  |  |  |
| --- | --- | --- | --- |
| **Target gene** | **Human** | **Pig** | **Mouse** |
| ***KCNN1*** | Hs01109326\_m1 | AJLJI7X\* | Mm01349167\_m1 |
| ***KCNN2*** | Hs01030641\_m1 | AJMSHD5\* | Mm00446514\_m1 |
| ***KCNN3*** | Hs01546821\_m1 | Ss03393243\_u1 | Mm00446516\_m1 |
| ***GAPDH*** | Hs02786624\_g1 | Ss03375629\_u1 | Mm99999915\_g1 |
| ***Rpl32*** | --- | --- | Mm02528467\_g1 |

Custom-designed TaqMan assays are indicated by an asterisk.

**Supplementary Reference**

1. Lugenbiel P, Wenz F, Syren P, Geschwill P, Govorov K, Seyler C et al. TREK-1 (K2P2.1) K+ channels are suppressed in patients with atrial fibrillation and heart failure and provide therapeutic targets for rhythm control. *Basic Res Cardiol* 2017;**112:**8.
2. Rahm AK, Wieder T, Gramlich D, Müller ME, Wunsch MN, El Tahry FA et al. HDAC2-dependent remodeling of KCa2.2 (KCNN2) and KCa2.3 (KCNN3) K+ channels in atrial fibrillation with concomitant heart failure. *Life Sci* 2021;**266:**118892.
3. Lugenbiel P, Govorov K, Syren P, Rahm AK, Wieder T, Wunsch M et al. Epigenetic regulation of cardiac electrophysiology in atrial fibrillation: HDAC2 determines action potential duration and suppresses NRSF in cardiomyocytes. *Basic Res Cardiol* 2021;**116:**13.
4. Rahm AK, Wieder T, Gramlich D, Müller ME, Wunsch MN, El Tahry FA et al. Differential regulation of KCa2.1 (KCNN1) K+ channel expression by histone deacetylases in atrial fibrillation with concomitant heart failure. *Physiol Rep* 2021;DOI: 10.14814/phy2.14835.