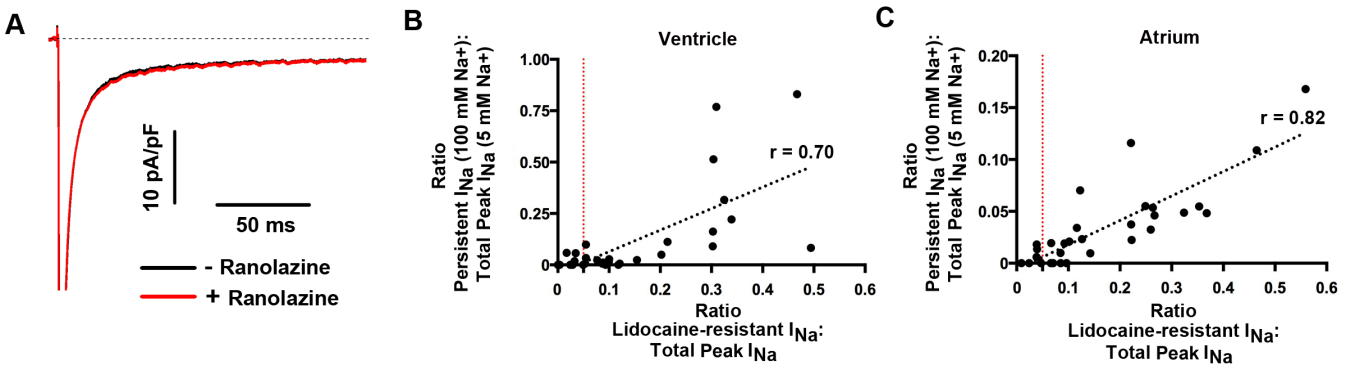
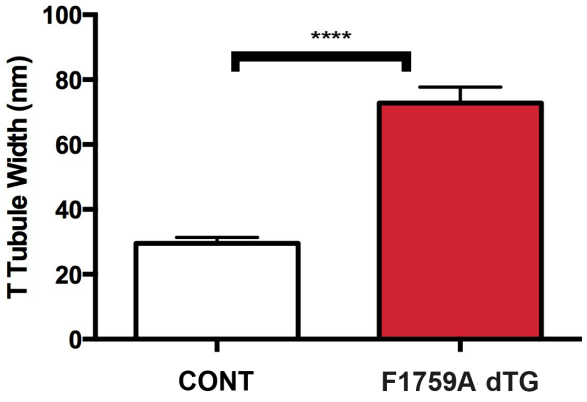
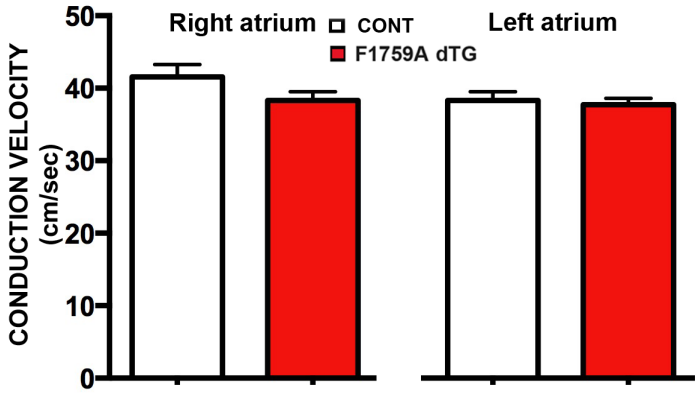


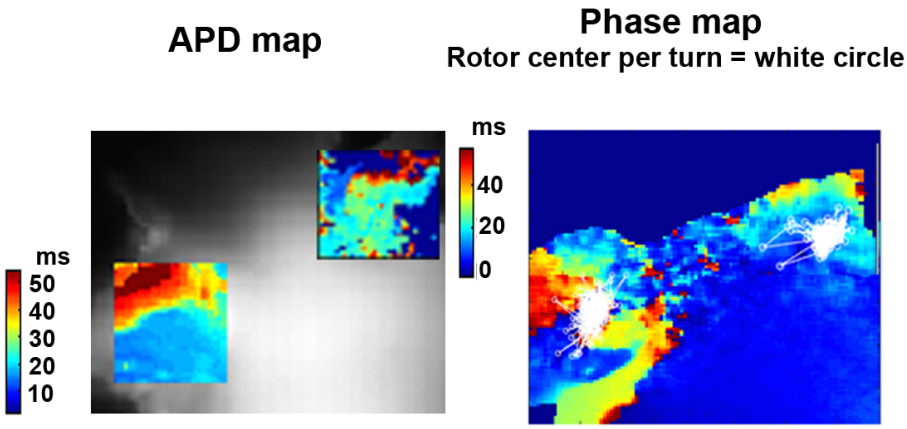
Supplemental Figure 1. Persistent Na^+ current in F1759A-dTG mice. (A) Exemplar whole cell Na^+ current traces of ventricular cardiomyocyte isolated from F1759A-dTG mice. Persistent Na^+ current was evaluated with a 190-ms depolarization from a holding potential of -110 mV to -30mV in the absence (black) and presence (red) of 50 μM ranolazine. The intracellular solution contained 5 mM Na^+ and the extracellular solution contained 100 mM Na^+. Persistent Na^+ current is resistant to 50 μM ranolazine in the F1759A-dTG mice. **(B-C)** The ratio of persistent Na^+ current to peak Na^+ current correlated with the ratio of lidocaine-resistant peak to total peak Na^+ current in atrial and ventricular cardiomyocytes isolated from F1759A dTG mice. Y-axis is ratio of persistent Na^+ current determined using 100 mM Na^+ in the extracellular solution to peak Na^+ current determined using 5 mM Na^+ in the extracellular solution. See methods. The vertical red dotted line corresponds to 5% residual peak Na^+ current after exposure to 3 mM lidocaine, representing the upper limit of lidocaine-resistance observed in control (NTG and single TG) mice. Ventricle: Pearson r = 0.70, *P* <0.0001; N= 31. Atrium: Pearson r = 0.82, *P* < 0.0001, N=30.



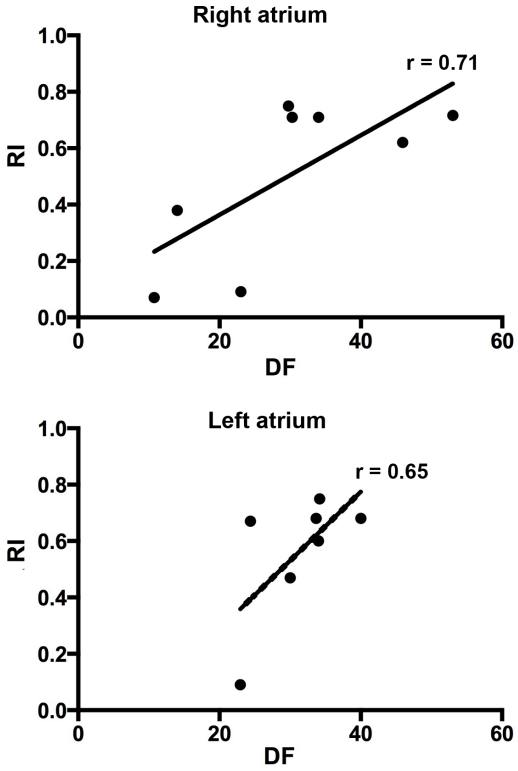
Supplemental Figure 2. T-tubule width is increased in F1759A-dTG mice. T-tubule width was determined in the ventricular sections of littermate control and F1759A-dTG at 12 weeks of age. ****, *P* <0.0001, *t*-test.



Supplemental Figure 3. Conduction velocity is equivalent in littermate control and F1759A-dTG mice. Mean + SEM. N= 3 for NTG mice. N= 3 for F1759A-dTG mice. *P* >0.05 *t*-test. Data, which were derived from the activation map in sinus rhythm, were processed by RHYTHM software (downloaded from I. Efimov laboratory website). The local conduction vectors were calculated from the smoothed atrial activation surface. Using the image size in cm, conduction velocity (cm/s) was calculated.



Supplemental Figure 4. Meandering of rotor core. APD (left) and phase (right) maps of Langendorff-perfused F1759A-dTG mouse heart with paroxysmal AF. The APD gradient map was obtained during the brief periods of sinus rhythm. Color legend of APD (ms) is shown to the left for right atrium and to the right for left atrium of APD map. A Matlab script was used to mark the location of the rotor core. Each white circle represents the position of the core every 10 frames of the phase movie (right column). The simultaneous right and left atrial rotors were independent.



Supplemental Figure 5. The regularity index (RI) is proportional to dominant frequency (DF) of AF. The RI is defined as the ratio of the power within a 1 Hz band centered on the DF and the total power spectrum from 0 to 100 Hz(*52*). DF was evaluated for each pixel as the frequency band with maximal power on a periodogram calculated with Fast-Fourier transform. Right atrium: Pearson r = 0.71, *P* <0.05, N=8. Left atrium: Pearson r = 0.65, *P* = 0.12, N=7.

Movies

Phase movies were generated by the RHYTHM software. 15 frames of optical signal were shown in 1 sec of the phase movie. Acquisitions of 1-2 seconds were recorded at a frequency of 1000 Hz. Movies 1 and 2 show simultaneous rotors in the right atrium and left atrium respectively.

Supplemental Movie 1. Rotor in right atrium. There is a stable rotor with slight meandering of the phase singularity, (+) chirality, a dominant frequency of 34 Hz and a regularity index of 0.75.

Supplemental Movie 2. Rotor in left atrium. There is a stable rotor with slight meandering of the phase singularity, (+) chirality, a dominant frequency of 30 Hz and a regularity index of 0.75.

Supplemental Movie 3. Simultaneous rotor in right atrium and wave reentry in left atrium. There is a right atrial rotor with a meandering phase singularity and (-) chirality that moves from the anterior surface to the posterior surface of the heart. Simultaneously, there is a left atrial wave reentry traversing medially to laterally.