SUPPLEMENTAL MATERIAL
SUPPLEMENTAL METHODS

Ventricular tachyarrhythmia (VT) vulnerability in *ex vivo* perfused hearts

After isolation, the heart was mounted on a Langendorff perfusion apparatus, and perfused with oxygenated (95% O₂ and 5% CO₂) modified Tyrode’s solution containing (in mM): 117 NaCl, 4.6 KCl, 1.0 MgCl₂, 23 NaHCO₃, 0.8 NaH₂PO₄, 2 CaCl₂ and 5.5 dextrose, equilibrated at 37°C. Ventricular epicardial electrograms were recorded by a bipolar electrode, placed on the epicardial surface of the LV apex. A bipolar pacing electrode was placed on the anterior epicardial surface of the right ventricle. VT induction was then attempted by programmed electrical stimulation at a PCL of 150 ms (S₁) with one to three (S₂, S₃, and S₄) extra-stimuli delivered after eight paced beats. The stimulation intensity was twice the threshold and 5 ms in duration. Pacing protocols were interrupted if sustained ventricular tachyarrhythmia was induced. The testing endpoint was inducing non-driven VTs. A preparation was considered noninducible when ventricular pacing produced either no ventricular premature beats or only self-terminating salvos of < 6 beats. Ventricular tachyarrhythmias including ventricular tachycardia and fibrillation were considered nonsustained when it lasted ≤ 15 beats and sustained when it lasted > 15 beats. An arrhythmia scoring system was used, as previously described: 0, noninducible preparations; 1, nonsustained tachyarrhythmias induced with three extrastimuli; 2, sustained tachyarrhythmias induced with three extrastimuli; 3, nonsustained tachyarrhythmias induced with two extrastimuli; 4, sustained tachyarrhythmias induced with two extrastimuli; 5, nonsustained tachyarrhythmias induced with one extrastimuli; 6, sustained tachyarrhythmias induced with one extrastimuli; and 7, tachyarrhythmias induced during the eight paced beats at a PCL of 150 ms. If the heart stopped before the pacing, the arrhythmia score assigned to that heart was 8. When multiple forms of arrhythmias occurred in one heart, the highest score was used.

Western blot analysis

Frozen LV tissues were homogenized in ice-cold lysis buffer. Protein concentration was measured using a Protein Assay Reagent (Bio-Rad Laboratories, Hercules, CA, USA) and adjusted for equal loading. Protein samples (30–100 µg) were separated on 4%–20% gradient gel (Mini-Protean®
Precast gels; Bio-Rad, Hercules, CA, USA; for RyR2, pSer<sup>2808</sup>-RyR2 or pSer<sup>2814</sup>-RyR2), 10% (SERCA2a, Kv4.2, Kv4.3, KChIP2, Kv1.4, Kv2.1, and Kir2.1), 15% (PLB, pSer<sup>16</sup>-PLB or pThr<sup>17</sup>-PLB), or 8% (NCX1, Cav<sub>1.2a</sub> or Nav1.5) SDS-PAGE and transferred onto PVDF membranes (PerkinElmer Life Sciences, Boston, MA, USA). Membranes were blocked and then incubated overnight at 4°C with primary antibody against RyR2 (mouse monoclonal, 1:1000; MA3-916, Thermo Fisher Scientific, MA, USA), pSer<sup>2808</sup>-RyR2 (rabbit polyclonal, 1:5000; A010-30AP, Baddrilla, Leeds, UK), pSer<sup>2814</sup>-RyR2 (rabbit polyclonal, 1:500; A010-31AP, Baddrilla), SERCA2a (rabbit polyclonal, 1:5000; A010-20, Baddrilla), PLB (mouse monoclonal, 1:2000; A010-14, Baddrilla), pSer<sup>16</sup>-PLB (rabbit polyclonal, 1:2000; 07-052, Millipore, Temecula, CA, USA), pThr<sup>17</sup>-PLB (rabbit polyclonal, 1:2000; A010-13, Baddrilla), NCX1 (rabbit polyclonal, 1:500; sc-30306; Santa Cruz Biotech, USA), Cav<sub>1.2a</sub> (rabbit polyclonal, 1:400; AB5156-50UL, Millipore), Nav1.5 (rabbit polyclonal, 1:500; ASC-005, Alomone labs, Jerusalem, Israel), Kv4.2 (rabbit polyclonal, 1:200; AB5360-200UL, Millipore), Kv4.3 (rabbit polyclonal, 1:200; APC-017, Alomone labs), Kv1.4 (rabbit polyclonal, 1:200; APC-007, Alomone labs), KChIP2 (rabbit polyclonal, 1:500; PA1-927, Thermo Fisher Scientific), Kv2.1 (rabbit polyclonal, 1:500; APC-012, Alomone labs), and Kir2.1 (rabbit polyclonal, 1:600; APC-026, Alomone labs). The blot was also probed by a GAPDH antibody (mouse monoclonal, 1:1000; sc-32233, Santa Cruz) or a β-actin antibody (rabbit polyclonal, 1:1000; ab8227, Abcam Inc., MA, USA) as an internal control. The membranes were then incubated with horseradish peroxidase-tagged anti-mouse IgG (1:5000, AP-124P, Millipore) or anti-rabbit IgG (1:10000, 111-035-003, Jackson ImmunoResearch Lab, Inc.) for 1 h at room temperature. The antibody-antigen complexes in all membranes were detected by the enhanced chemiluminescence detection kit (PerkinElmer) according to the manufacturer’s instructions and digitized in a BioSpectrum 500 Imaging System (UVP, Upland, CA, USA). The densities of the immunoreactive bands were quantified using VisionWorks LS image software (version 6.6a; UVP).

**Whole-cell patch-clamp recording**
**Pulse protocol and analysis**

\(K^+\) currents were elicited with depolarizing or hyperpolarizing steps from a holding potential of –80 mV to test potentials ranging between –140 and +60 mV (20-mV steps, 400-ms duration) with a stimulation frequency of 0.2 Hz. Voltages more positive than –30 mV activated a peak outward \(K^+\) current and subsequently inactivated to a sustained level (\(I_{SS}\)) at the end of the pulse. A rapidly activating and inactivating \(I_{to}\) was identified as the difference between the peak and the steady-state current (\(I_{SS}\)). Voltages negative to –60 mV activated an inward current that represented the inward rectifier \(K^+\) current (\(I_{K1}\)). To obtain the steady-state inactivation curves of \(I_{to}\), a double-pulse protocol was used. The membrane was voltage-clamped to different conditioning potentials (from –90 to +10 mV) for 200 ms and then stepped to +60 mV for 100 ms, at which time \(I_{to}\) was fully activated. The holding potential was –80 mV, and the interval between test pulses was 5 s. The relative peak amplitudes of \(I_{to}\) (\(I_{to}/I_{to, max}\)) were plotted against prepulse potentials, and fitted to Boltzmann function and the voltage for half-inactivation (\(V_h\)) and slope factor (\(k\)) were calculated. To obtain the recovery curves of \(I_{to}\) from inactivation, a paired-pulse protocol was used consisting of two identical 200-ms depolarizing pulses to +60 mV from a holding potential of –80 mV. The prepulse–test pulse interval was varied between 10 and 550 ms. Each paired-pulse sequence was separated by a 10-s interval to allow for complete recovery of \(I_{to}\) from inactivation. The normalized recovery fraction of \(I_{to}\) (\(I_{test\ pulse}/I_{prepulse}\)) was plotted against the recovery times and fitted to a monoexponential function.

L-type \(Ca^{2+}\) currents (\(I_{Ca,L}\)) were evoked by applying the depolarizing steps to test potentials ranging between –40 and +60 mV (10-mV steps, 250-ms duration) from a holding potential of –80 mV, after a 150-ms prepulse to –40 mV to inactivate \(I_{Na}\) and T-type \(Ca^{2+}\) current. Steady-state inactivation of \(I_{Ca,L}\) was examined with a double-pulse protocol: 1-s conditioning pulses were applied in 10-mV steps between –70 to +20 mV from a holding potential of –80 mV, and then the test pulse of 200-ms duration was applied to 0 mV after a 30-ms interpulse to –40 mV. The relative peak amplitudes of \(I_{Ca,L}\) were plotted against prepulse potentials and fitted to Boltzmann distribution. To obtain the recovery curves of \(I_{Ca,L}\) from inactivation, a paired-pulse protocol was used consisting of
two identical 250-ms depolarizing pulses to 0 mV from a holding potential of –40 mV. The prepulse–test pulse interval was varied between 40 and 4050 ms. Each paired-pulse sequence was separated by a 10-s interval to allow for complete recovery of $I_{Ca,L}$ from inactivation. The normalized recovery fraction of $I_{Ca,L}$ ($I_{test pulse}/I_{prepulse}$) was plotted against the recovery times and fitted to a bi-exponential function.

$Na^+$ inward currents ($I_{Na}$) were evoked by applying the depolarizing steps to test potentials ranging between –70 and +40 mV (10-mV steps, 30-ms duration) from a holding potential of –100 mV. Steady-state inactivation of $I_{Na}$ was examined with a double-pulse protocol: 1-s conditioning pulses were applied in 10-mV steps between –140 to –40 mV from a holding potential of –80 mV, and then the test pulse of 50-ms duration was applied to –20 mV. To obtain the recovery curves of $I_{Na}$ from inactivation, a paired-pulse protocol was used. A 50-ms prepulse was first applied from a holding potential of –100 mV to –20 mV, which was followed by a 20 ms test pulse after variable interpulse intervals ranging from 10 to 580 ms. The normalized recovery curve was fitted to a monoexponential function.

Steady-state inactivation data of voltage-activated ion channels were fitted with a Boltzmann function of the form:

$$\frac{I}{I_{max}} = \frac{1}{1+\exp\left[(V_m-V_h)/k\right]}$$

where $I$ gives the current amplitude and $I_{max}$ its maximum, $V_m$ the potential of prepulse, $V_h$ the half-maximal inactivation potential, and $k$ the slope factor. Conductance of voltage-activated ion channel ($G$) was calculated according to the equation as follows:

$$G = \frac{I}{(V_m-V_{rev})}$$

where $I$ is the peak ionic current, $V_{rev}$ is the reversal potential of this current (approximately –80 mV for $I_{lo}$, +70 mV for $I_{Ca,L}$, and +40 mV for $I_{Na}$), and $V_m$ is the test potential. The normalized $G$ ($G/G_{max}$) was plotted as a function of $V_m$ (activation curve) and analyzed by using the Boltzmann equation as follows:

$$\frac{G}{G_{max}} = \frac{1}{1+\exp\left[(V_h-V_m)/k\right]}$$
where $G_{\text{max}}$ is the maximal ionic conductance, and $V_h$ and $k$ represent the half-maximal activation potential and a slope factor, respectively.
Table S1. Kinetic parameters of current decay, steady-state activation and inactivation, and recovery of $I_{Ca,L}$ in ventricular myocytes isolated from various group rats

|                | Sham+Veh | AB+Veh | Sham+Can | AB+Can |
|----------------|----------|--------|----------|--------|
| **Decay**      |          |        |          |        |
| n              | 10       | 11     | 10       | 10     |
| $\tau_1$ (ms)  | 12.8 ± 5.5 | 19.0 ± 7.3 | 15.4 ± 5.1 | 14.3 ± 7.9 |
| $\tau_2$ (ms)  | 66.0 ± 17.8 | 95.5 ± 57.8 | 64.8 ± 16.1 | 88.8 ± 30.2 |
| **Activation** |          |        |          |        |
| n              | 10       | 11     | 10       | 10     |
| $G_{\text{max}}$ (pS/pF) | 130.0 ± 39.5 | 125.3 ± 39.7 | 131.0 ± 30.8 | 138.5 ± 27.5 |
| $V_h$ (mV)     | −17.4 ± 4.4 | −19.0 ± 4.3 | −18.2 ± 1.9 | −20.3 ± 4.0 |
| $k$ (mV)       | 5.0 ± 1.0 | 4.5 ± 0.9 | 4.7 ± 1.0 | 4.0 ± 1.2 |
| **Inactivation**|          |        |          |        |
| n              | 9        | 10     | 9        | 10     |
| $V_h$ (mV)     | −34.0 ± 4.7 | −31.1 ± 7.2 | −33.2 ± 5.1 | −28.9 ± 3.8 |
| $k$ (mV)       | −5.8 ± 1.3 | −5.8 ± 0.7 | −5.8 ± 0.8 | −6.0 ± 0.9 |
| **Recovery**   |          |        |          |        |
| n              | 9        | 9      | 8        | 11     |
| $A_f$          | 0.56 ± 0.15 | 0.69 ± 0.16 | 0.61 ± 0.20 | 0.70 ± 0.26 |
| $\tau_f$ (s)   | 0.20 ± 0.13 | 0.20 ± 0.09 | 0.19 ± 0.10 | 0.21 ± 0.08 |
| $\tau_s$ (s)   | 1.12 ± 0.76 | 1.66 ± 1.22 | 1.78 ± 1.50 | 1.23 ± 0.39 |

Data are presented as means±SD. n is number of experiments. Veh indicates vehicle; AB, aortic banding; Can, candesartan cilexetil; $G_{\text{max}}$, maximal conductance; $\tau_1$ and $\tau_2$, fast and slow time constant for channel inactivation at 0 mV, respectively; $V_h$ and $k$, half-activation or inactivation voltage and slope factor, respectively; $A_f$, the fast fraction of channel recovery; $\tau_f$ and $\tau_s$, fast and slow time constant for channel recovery, respectively. Data were analyzed by linear mixed model analysis.
Table S2. Kinetic parameters of current decay, steady-state activation and inactivation, and recovery of peak $I_{Na}$ in ventricular myocytes isolated from various group rats

|                | Sham+Veh | AB+Veh | Sham+Can | AB+Can |
|----------------|----------|--------|----------|--------|
| **Decay**      |          |        |          |        |
| $n$            | 14       | 16     | 12       | 12     |
| $\tau_1$ (ms)  | $1.66 \pm 0.84$ | $1.62 \pm 0.89$ | $1.87 \pm 0.80$ | $1.46 \pm 0.85$ |
| $\tau_2$ (ms)  | $5.60 \pm 5.51$ | $5.17 \pm 2.87$ | $5.87 \pm 4.00$ | $4.34 \pm 4.03$ |
| **Activation** |          |        |          |        |
| $n$            | 14       | 16     | 12       | 12     |
| $G_{max}$ (pS/pF) | $296.7 \pm 111.5$ | $262.3 \pm 96.8$ | $344.7 \pm 193.6$ | $317.4 \pm 119.5$ |
| $V_h$ (mV)     | $-43.2 \pm 7.3$ | $-45.4 \pm 11.3$ | $-41.6 \pm 7.9$ | $-45.8 \pm 7.9$ |
| $k$ (mV)       | $3.0 \pm 2.0$ | $2.2 \pm 0.8$ | $3.6 \pm 2.4$ | $2.1 \pm 1.0$ |
| **Inactivation** |          |        |          |        |
| $n$            | 14       | 16     | 12       | 12     |
| $V_h$ (mV)     | $-81.8 \pm 12.0$ | $-84.8 \pm 10.3$ | $-81.2 \pm 11.4$ | $-79.6 \pm 9.1$ |
| $k$ (mV)       | $-6.8 \pm 1.3$ | $-6.5 \pm 1.0$ | $-6.8 \pm 1.6$ | $-6.2 \pm 0.7$ |
| **Recovery**   |          |        |          |        |
| $n$            | 12       | 14     | 11       | 11     |
| $\tau$ (ms)    | $22.0 \pm 18.4$ | $32.7 \pm 15.9$ | $24.6 \pm 10.9$ | $27.4 \pm 19.6$ |

Data are presented as means±SD. $n$ is number of experiments. Veh indicates vehicle; AB, aortic banding; Can, candesartan cilexetil; $G_{max}$, maximal conductance; $\tau_1$ and $\tau_2$, fast and slow time constant for channel inactivation at $-30$ mV, respectively; $V_h$ and $k$, half-activation or inactivation voltage and slope factor, respectively; $\tau$, time constant for channel recovery. Data were analyzed by linear mixed model analysis.
A, Representative photomicrographs of hematoxylin and eosin-stained cross-sectional sections of LV (upper panel) and left atrial (lower panel) free walls from rats of each group. B, Mean cardiomyocyte diameter of LV free walls calculated from sections of Sham (S)+vehicle (Veh) (n=90 myocytes/9 rats), aortic banding (AB)+Veh (n=90/9), S+candesartan cilexetil (Can) (n=80/8), and AB+Can (n=90/9) group rats. C, Mean cardiomyocyte diameter of left atrial free walls calculated from sections of Sham+Veh (n=60 myocytes/6 rats), AB+Veh (n=68/6), Sham+Can (n=67/7), and AB+Can (n=55/6) group rats. Data are presented as means±SD. #P<0.001 vs. Sham+Veh group; ‡P<0.01 and $P<0.001 vs. AB+Veh group by linear mixed model analysis.
A, Representative images of Masson’s trichrome-stained sections (×200) of left ventricular (LV, upper panel) and left atrial (LA, lower panel) free walls from rats of each group. Collagen (fibrosis) is stained blue. B and C, Mean interstitial fibrosis area of LV (B) and LA (C) free walls calculated from sections of Sham (S)+vehicle (Veh) (n=9 rats in LV and 8 rats in LA), aortic banding (AB)+Veh (n=9 both in LV and LA), S+candesartan cilexetil (Can) (n=8 both in LV and LA), and AB+Can (n=9 both in LV and LA) groups. Data are presented as means±SD. *P<0.05 and #P<0.001 vs. Sham+Veh group; †P<0.05 and ‡P<0.01 vs. AB+Veh group by one-way ANOVA with a Tukey’s post hoc test.
A. Representative superimposed action potential traces obtained from left atrial strips stimulated at 1 or 4 Hz. B–G, Effects of increased stimulus frequency (0.5–4 Hz) on action potential duration (APD) at the 25%, 50%, and 90% repolarization levels (APD_{25, 50, 90}), maximal depolarization velocity (dV/dt_{max}), action potential amplitude, or resting membrane potential (RMP) in all groups. Veh indicates vehicle; AB, aortic banding; Can, candesartan cilexetil. Values are presented as means±SD. Data were analyzed by two-way ANOVA.
**Figure S4.** Transmembrane action potential variables recorded in central subepicardial and subendocardial sites of left ventricular (LV) free wall slices isolated from various group hearts.

**A,** Schematic diagram of a LV free wall slice preparation (0.2 mm thickness) isolated from a vehicle-treated banded rat. A microelectrode (arrow) was used to record transmembrane action potential from subepicardial (Epi) or subendocardial (Endo) site. **B,** Representative action potentials obtained from Epi (upper panel) and Endo (lower panel) sites from various group hearts. Stimulus frequency was 1 Hz. **C–E,** Averaged action potential duration (APD) variables at the 25%, 50%, and 90% repolarization levels (APD$_{25}$, 50, and 90) calculated from subepicardial and subendocardial action potentials in all groups. Veh indicates vehicle; AB, aortic banding; Can, candesartan cilexetil. Values are presented as means±SD. *$P<0.05$ and **$P<0.01$ vs. Sham+Veh group; †$P<0.05$ vs. AB+Veh group by one-way ANOVA with a Tukey’s post hoc test.
Figure S5. NADPH-dependent superoxide anion production in left ventricular (LV) and left atrial (LA) tissues from various group hearts.

Mean value of relative superoxide production of LV (A) and LA (B) free walls from 8 rats in each group. S indicates sham; Veh, vehicle; AB, aortic banding; Can, candesartan cilexetil. Data are presented as means±SD. Value is expressed relative to Sham+Veh group. **P<0.01 vs. Sham+Veh group and †P<0.05 vs. AB+Veh group by one-way ANOVA with a Tukey’s post hoc test.
A. Sample current tracings obtained in left ventricular (LV) myocytes from Sham+Veh (194 pF), Sham+Can (174 pF), AB+Veh (306 pF), and AB+Can (268 pF) groups. $I_{Ca,L}$ traces were elicited by applying a series of 250-ms long step pulses between –40 and +70 mV from a holding potential of –80 mV, after a prepulse to –40 mV to inactivate $I_{Na}$ and T-type Ca$^{2+}$ current. Veh indicates vehicle; AB, aortic banding; Can, candesartan cilexetil. B, Averaged $I$–$V$ relationships of $I_{Ca,L}$ in myocytes from various group rats. The amplitude of $I_{Ca,L}$ was measured as the difference between the peak current and the current at the end of the pulse. Each data point represents means± SD from Sham+Veh (n=10 cells/4 rats; Cm=204±44 pF), Sham+Can (n=10/5; Cm=242±58 pF), AB+Veh (n=11/4; Cm=304±65 pF), and AB+Can (n=10/4; Cm=262±32 pF) rats. C, Voltage dependence of activation (Act.) and steady-state inactivation (Inac.) of $I_{Ca,L}$ from various group myocytes. The activation curves were derived using $I$–$V$ curves shown in panel B. Steady-state inactivation was examined with a
double pulse protocol (inset): 1-s conditioning pulses were applied in 10 mV steps between –70 mV and +20 mV from a holding potential of –80 mV, and then the test pulse of 200-ms duration was applied to 0 mV (interpulse duration was 30 ms). Line curves shown are fits of mean data by Boltzmann distribution. Each point is the means±SD from individual group cells. The number of myocytes/rats used for activation and inactivation studies are 10/5 and 9/4, 10/4 and 9/4, 11/5 and 10/4, and 10/4 and 10/4, respectively, in Sham+Veh, Sham+Can, AB+Veh, and AB+Can rats. D, Time course of recovery from inactivation of $I_{Ca,L}$ in myocytes from Sham+Veh (n=9 cells/4 rats), Sham+Can (n=8/4), AB+Veh (n=9/4), and AB+Can (n=11/5) group rats. Recovery was determined with the paired-pulse protocol as shown in the inset. The normalized recovery fraction of $I_{Ca,L}$ ($I_{test\ pulse}/I_{prepulse}$) was plotted against the recovery times. Each curve was adequately fit by a bi-exponential function. Data were analyzed by linear mixed model analysis.
Figure S7. Comparison of peak Na⁺ current ($I_{\text{Na}}$) among various groups.

A. Sample current tracings obtained in left ventricular (LV) myocytes from Sham+Veh (160 pF), Sham+Can (173 pF), AB+Veh (249 pF), and AB+Can (209 pF) groups. Peak $I_{\text{Na}}$ traces were evoked by applying the depolarizing steps to test potentials ranging between $-70$ and $+40$ mV (10-mV steps, 30-ms duration) from a holding potential of $-100$ mV. Veh indicates vehicle; AB, aortic banding; Can, candesartan cilexetil.

B. Averaged $I$–$V$ relationships of peak $I_{\text{Na}}$ in myocytes from various group rats. The amplitude of peak $I_{\text{Na}}$ was measured as the difference between the peak current and the current at the end of the pulse.

C. Voltage dependence of activation (Act.) and steady-state inactivation (Inac.) of peak $I_{\text{Na}}$ from various group myocytes. The activation curves were derived using $I$–$V$ curves shown in panel B. Steady-state inactivation of peak $I_{\text{Na}}$ was examined with a double-pulse protocol: 1-s conditioning pulses were applied in 10-mV steps between $-140$ to $-40$ mV from a holding potential of $-80$ mV, and then the test pulse of 50-ms duration was applied to $-20$ mV. Line curves shown are fits of mean data by Boltzmann distribution. Data in panels B–C are presented as means±SD from
Sham+Veh (n=14 cells/4 rats; Cm=220±46 pF), Sham+Can (n=12/4; Cm=196±56 pF), AB+Veh (n=16/6; Cm=258±72 pF), and AB+Can (n=12/5; Cm=234±95 pF) rats. D, Time course of recovery from inactivation of peak $I_{Na}$ in myocytes from Sham+Veh (n=12 cells/4 rats), Sham+Can (n=11/4), AB+Veh (n=14/5), and AB+Can (n=11/5) rats. Recovery was determined with the paired-pulse protocol as shown in the inset. A 50-ms prepulse was first applied from a holding potential of $-100$ mV to $-20$ mV, which was followed by a 20 ms test pulse after variable interpulse intervals ranging from 10 to 580 ms. The normalized recovery fraction of peak $I_{Na}$ ($I_{test pulse}/I_{prepulse}$) was plotted against the recovery times. Each curve was adequately fit by a monoeponential function. Data were analyzed by linear mixed model analysis.
Bars represent means±SD of relative mRNA of Kv4.2 (A) and Kv4.3 (B) in LV tissues from 7 rats in each group. All measurements were normalized to the levels of GAPDH. S indicates sham; Veh, vehicle; AB, aortic banding; Can, candesartan cilexetil. Value is expressed relative to Sham+Veh group. #P < 0.001 vs. Sham+Veh group and ‡P < 0.01 vs. AB+Veh group by one-way ANOVA with a Tukey’s post hoc test.