Electrophysiological properties of cardiac-like cells in the pulmonary vein

Sunil Jit Logantha, Robert M. Drummond, Edward G. Rowan

University of Strathclyde, Glasgow, United Kingdom

The pulmonary vein of many species is surrounded by a sleeve of cardiac-like cells that can extend from the atrium to deep within the lung (Best *et al*., 1961). These cardiac-like cells are known to be a source of ectopic electrical activity capable of triggering atrial arrhythmias (Haissaguerre *et al*., 1998). It is therefore important to understand the electrical properties of these cells. The aim of this study was to determine whether cardiac-like cells of the rat pulmonary vein show spontaneous electrical activity and whether or not this is related to changes in the intracellular Ca^{2+} concentration.

Male Sprague Dawley rats (180-300 g) were killed by cervical dislocation and the pulmonary vein carefully dissected. For electrophysiological studies, membrane potentials were recorded from cardiac-like cells in bath solution (in mM; NaCl, 150; KCl, 5.4; HEPES, 10; Glucose, 10; $MgCl_2$, 1.2; $CaCl_2$, 1.8 and adjusted to pH 7.4) using conventional microelectrode techniques. Electrical field stimulation was carried out using a pair of platinum electrodes. For Ca^{2+} imaging, the tissue was loaded with 10 μM fluo-4 AM in the presence of 0.03 % cremophor and imaged using a Hamamatsu CCD camera. All experiments were carried out at room temperature. Data are presented as mean ± SEM and n is the number of cardiac-like cells studied. Repeated measures one way ANOVA with Tukey multiple comparisons post-test was used for statistical comparison. The difference was considered significant at $P < 0.05$.

Cardiac-like cells had a stable resting membrane potential of -72.83 ± 1.38 mV (n = 20) with no evidence of any spontaneous electrical activity. Following field stimulation, action potentials could be elicited in these cells. The peak amplitude of the action potentials was 72.41 ± 3.12 mV and the time taken for 90% repolarization (T_{90}) was 40.49 ± 4.34 ms (n = 20). A decrease in the peak amplitude and T_{90} of action potentials occurred on increasing the frequency of stimulation. At 7 Hz the amplitude and T_{90} were significantly lower at 53.44 ± 7.45 mV (n=8, $P<0.05$) and 24.32 ± 4.96 ms (n=8, $P<0.01$) respectively. Also, at 7 Hz action potentials failed to follow every stimuli in 5 out of 8 vein preparations. The action potentials were completely blocked by 10 μM nicardipine. Fluorescence Ca^{2+} imaging of cardiac-like cells revealed that electrical field stimulation evoked global increases in intracellular Ca^{2+} that were uniform throughout all cells in the field of view. In the absence of electrical field stimulation, spontaneous Ca^{2+} transients occurred within individual cardiac-like cells. These transients were asynchronous in nature with a frequency of 1.4 ± 0.04 Hz and amplitude of 0.11 ± 0.01 $\Delta F/F_{min}$ (n = 141) and appear to be due to Ca^{2+} release from the sarcoplasmic reticulum.

Whilst the above studies show that there are no spontaneous changes in the membrane potential, action potentials can be evoked by electrical field stimulation in the cardiac-like cells. These action potentials are mediated by influx of Ca^{2+} through voltage operated Ca^{2+} channels and are capable of producing global increases in intracellular Ca^{2+}.

Best PV *et al*. (1961). *Circ Res* 9, 288-294.

Haïssaguerre M *et al*. (1998). *N Engl J Med* 339, 659-666.