

## Voltage and current clamp recordings of Cor.4U® human iPS cell-derived cardiomyocytes on Nanion's Patchliner®

The electrophysiology team at Nanion Technologies GmbH, Munich.  
Cells kindly provided by Axiogenesis AG.



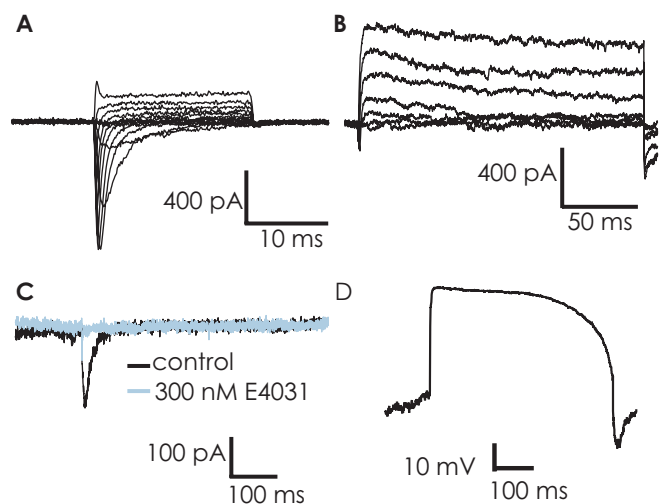
### Summary

Although mouse embryonic stem (ES) cell-derived cardiomyocytes, e.g. Cor.At® cells from Axiogenesis, can provide a useful model for drug discovery and safety testing as an alternative to acutely dissociated rat or mouse cardiomyocytes, human induced pluripotent (iPS) cell-derived cardiomyocytes have the potential to provide the ultimate model system for identifying potential anti-arrhythmic effects of drugs during routine safety screening. Axiogenesis has now launched the Cor.4U® human iPS cell-derived cardiomyocyte product line for use in testing the efficacy and safety of pharmaceutical therapies. The ability to characterize the ion channel profile of these cells and reliably record action potentials at a reasonable throughput is essential to fully realise the potential of this kind of product line. Building on the success of Cor.At® mouse embryonic stem (ES) cell-derived cardiomyocytes on the Patchliner®<sup>1,2</sup>, Cor.4U® human iPS cell-derived cardiomyocytes have now been characterized on the Patchliner® in the voltage and current clamp modes.

In this Application Note we present data using an 8-channel Patchliner® characterizing Cor.4U® cells. In the voltage clamp mode, voltage-dependent Na<sup>+</sup> ( $I_{Na}$ ), K<sup>+</sup> ( $I_K$ ) and hERG (an inward current using a high K<sup>+</sup>-containing external solution) channel currents were recorded (Fig. 1). When the Ca<sup>2+</sup> channel agonist BayK 8644 was used a voltage-gated Ca<sup>2+</sup> ( $I_{Ca}$ ) current could be recorded (Fig. 2). As expected, action potentials could be elicited in the current clamp mode (Fig. 3). The effect of the compounds TTX and BayK8644 on the action potentials evoked in Cor.4U cells is also shown (Fig. 3).

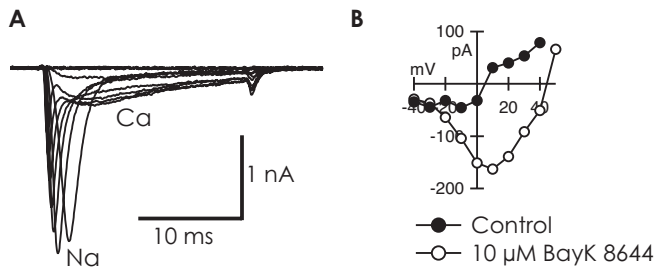
### Results

Figure 1 shows recordings in the voltage clamp mode of Cor.4U® cells exhibiting Na<sub>v</sub> (A) and K<sub>v</sub> (B) currents. An inward K<sup>+</sup> current was observed when using an external solution containing high K<sup>+</sup> (C). This is confirmed to be hERG by the use of the specific antagonist E4031. In the current clamp mode, spontaneous action potentials (AP) could be seen (D). Figure 2 shows both Na<sup>+</sup> and Ca<sup>2+</sup> currents as recorded in the voltage clamp mode. Furthermore, the Ca<sup>2+</sup> channel agonist BayK 8644 increases Ca<sup>2+</sup> channel mediated currents.



**Figure 1:** Currents recorded from Cor.4U® cells. **A** Na<sub>v</sub> current, **B** K<sub>v</sub> current and **C** hERG inward current (recorded in the presence of high external K<sup>+</sup>) and block by E4031. Spontaneous AP as recorded in the current clamp mode.

# Application Note



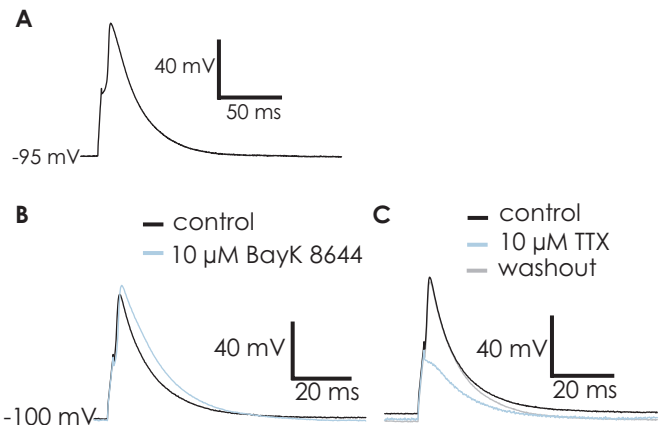
**Figure 2:**

**A** Raw data traces as recorded in the voltage clamp mode showing  $\text{Na}^+$  and  $\text{Ca}^{2+}$  inward currents. **B**  $\text{Ca}^{2+}$  channel mediated currents in Cor.4U cells could be increased using BayK 8644. IV plot in control conditions (closed circles) and in the presence of BayK 8644 (open circles), raw data traces not shown.

Figure 3 shows action potentials recorded from Cor.4U<sup>®</sup> cells recorded in the current clamp mode in control conditions (A) and in the presence of compounds BayK 8644 and TTX (B, C). BayK 8644 elicits a lengthening of the duration of the AP (B) and TTX abolishes the AP (C). This effect is reversible upon washout of TTX.

In conclusion, Cor.4U<sup>®</sup> cells exhibit the ion channel profile ( $\text{Na}_v$ ,  $\text{K}_v$ ,  $\text{Ca}_v$  and hERG) expected in human

cardiomyocytes. These ion channels expressed in conjunction contribute to the action potentials which are elicited in these cells. The compounds BayK 8644 and TTX modify the action potentials as expected.



**Figure 3:**

Action potentials recorded from Cor.4U<sup>®</sup> cells in the current clamp mode. **A** In control conditions, **B** In the presence of BayK 8644 and **C** in the presence of TTX.

The data provide evidence that the Patchliner<sup>®</sup> is well suited to recording Cor.4U<sup>®</sup> cells in a higher throughput environment given its flexibility and reliability.

## References

1. Stoelzle *et al.*, 2011. JBS. 16 (8): 910–916
2. Stoelzle *et al.*, 2011. Front Pharmacol. 2 (76) doi: 10.3389/fphar.2011.00076

## Methods

### Cells

Cor.4U<sup>®</sup> cells were supplied by Axiogenesis AG.

### Cell culture

Cells were cultured and harvested according to Nanion's standard cell culture protocol for stem cell-derived cardiomyocytes.

## Electrophysiology

Whole cell recordings were conducted according to Nanion's standard procedure for the Patchliner<sup>®</sup>. Current-voltage recordings were made using voltage steps from -60 mV to 50 mV for 20 ms increasing in 10 mV steps, from a holding potential of -120 mV ( $\text{Na}_v$ ); -60 mV to 60 mV for 200 ms increasing in 20 mV steps from a holding potential of -80 mV ( $\text{K}_v$ ); -40 mV to 50 mV for 100 ms increasing in 10 mV steps from a holding potential of -100 mV ( $\text{Ca}_v$ ; in the presence or absence of 10 μM BayK 8644). Inward hERG current was elicited by stepping from the pre-pulse +40 mV to -120 mV using an external solution containing 126 mM  $\text{K}^+$ . APs were elicited using a 1 ms current pulse to the threshold necessary to generate an action potential in each cell (calculated for each cell individually).