Application Note

Channel: I_{Na}, I_K, I_{Ca}
Cells: human iPS cardiomyocytes
Tools: Patchliner®

Voltage and current clamp recordings of Cellartis® hiPS-CM on Nanion's Patchliner®

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Cells kindly provided by Takara Bio Europe AB.

cellartis BY TAKARA BIO

Summary

Human induced pluripotent stem (iPS) cell-derived cardiomyocytes have the potential to provide the ultimate model system for identifying potential anti-arrythmic effects of drugs during routine safety screening. Takara Bio Europe AB is providing a 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 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 recording stem cells on the Patchliner®[1-3], Cellartis® hiPS-CM, human iPS cell-derived cardiomyocytes, have now been characterized on the Patchliner® in the voltage and current clamp mode.

In this Application Note we present data using an 8-channel Patchliner®. In the voltage clamp mode, voltage-dependent Na^+ (Na_V), K^+ (K_V) and Ca^{2+} (Ca_V) channel currents were recorded.
As expected, action potentials could be elicited in the current clamp mode. Furthermore, spontaneous action potentials could be recorded as well.

Seal Resistance	C_{slow}	R_s
1,1 ± 0,19 GΩ	18,6 ± 2 pF	7,8 ± 3 mV

Table 1:
Sucess rate of Cellartis® hiPS-CM (Takara Bio Europe AB) as recorded on an 8-channel Patchliner equipped with temperature control.

Results

Figure 1 shows recordings in the current and voltage clamp mode of Cellartis® hiPS-CM. Current traces show exemplary Na_V and Ca_V currents. In the same cell, recorded in the current clamp mode, action potentials (AP) could be elicited. Figure 2 shows raw data traces and current-voltage relations of Na^+ and K^+ currents as recorded in the voltage clamp mode.

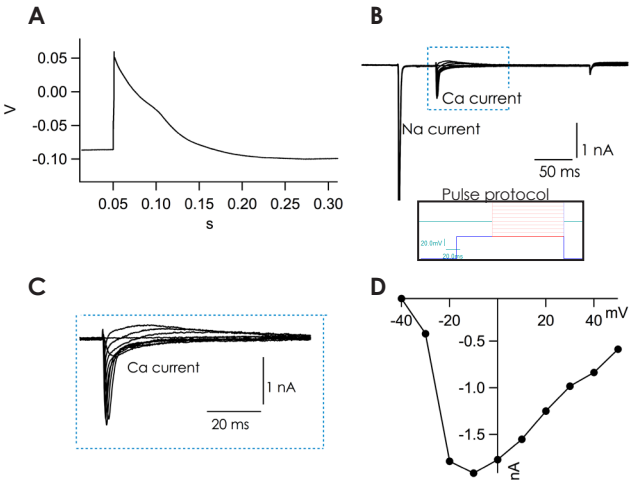

Figure 1:
Currents recorded from Cellartis® hiPS-CM (Takara Bio Europe AB). **A** Elicited AP as recorded in the current-clamp mode. **B** Na_V and Ca_V current in the voltage clamp mode. The inset shows the applied voltage pulse protocol. **C** Zoom-in to Ca currents, corresponding current-voltage relation (**D**).

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Application Note

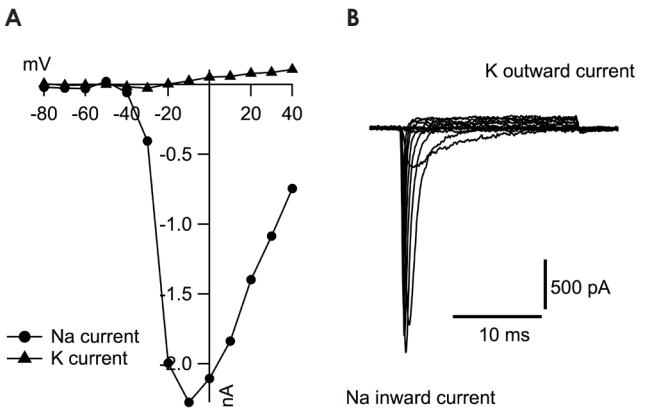

Figure 2:
A Current-voltage relation of Na channel mediated currents (circles) and K outward current (triangles). **B** Raw data traces as recorded in the voltage clamp mode showing Na^+ and K^+ currents.

Figure 3 shows action potentials from Cellartis® hiPS-CM recorded in the current clamp mode. Here, the APs were either induced (arrow at x-axis represents timepoint of stimulus) or occured spontaneously.

In conclusion, human induced pluripotent stem (iPS) cell-derived cardiomyocytes from Takara Bio Europe AB exhibit an ion channel profile (Na_V, K_V, Ca_V) as expected in human cardiomyocytes. These ion channels expressed in conjunction contribute to the action potentials which are elicited in these cells.

The data provide evidence that the Patchliner® is well suited to recording stem cell-derived cardiomyocytes in a higher throughput environment given its flexibility and reliability.

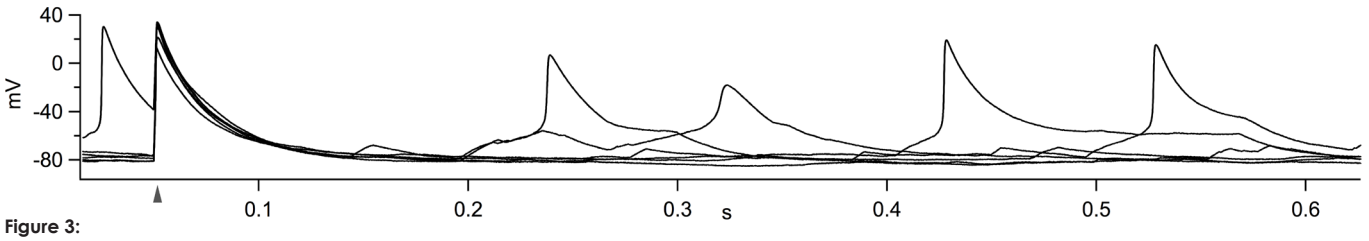

Figure 3:
Induced and spontaneous action potentials recorded from Cellartis® hiPS-CM (Takara Bio Europe AB) in the current clamp mode. Arrow in the x-Axis represents timepoint of applied stimulus.

References

1. Becker et al., 2013, Jpharmtox, JPM-06117
2. Stoelzle *et al.*, 2011. JBS. 16 (8): 910–916
3. Stoelzle *at al.*, 2011. Front Pharmacol. 2 (76) doi: 10.3389/fphar.2011.00076

Methods

Cells

human iPS cell-derived cardiomyocytes (Cellartis® hiPS-CM) were supplied by Takara Bio Europe AB.

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®. 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 (Na_V); -40 mV to 50 mV for 200 ms increasing in 10 mV steps from a holding potential of -100 mV (Ca_V), a 50 ms pre-pulse to -40 mV inactivated Na currents. APs were elicited using a 1 ms current pulse (calculated for each cell individually).

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