Zebrafish heart as a model for human cardiac electrophysiology

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ABSTRACT
The zebrafish (Danio rerio) has become a popular model for human cardiac diseases and pharmacology including cardiac arrhythmias and its electrophysiological basis. Notably, the phenotype of zebrafish cardiac action potential is similar to the human cardiac action potential in that both have a long plateau phase. Also the major inward and outward current systems are qualitatively similar in zebrafish and human hearts. However, there are also significant differences in ionic current composition between human and zebrafish hearts, and the molecular basis and pharmacological properties of human and zebrafish cardiac ionic currents differ in several ways. Cardiac ionic currents may be produced by non-orthologous genes in zebrafish and humans, and paralogous gene products of some ion channels are expressed in the zebrafish heart. More research on molecular basis of cardiac ion channels, and regulation and drug sensitivity of the cardiac ionic currents are needed to enable rational use of the zebrafish heart as an electrophysiological model for the human heart.

Introduction
Zebrafish, a tropical teleost fish species is increasingly used as a model for human cardiac electrophysiology, arrhythmias and drug screening.6,12,53,56 The use of zebrafish models is based, besides the several well established technical advantages (optical transparency, large offspring number, rapid development, genetic amenability), on the promise that genetic and molecular mechanisms behind cardiac physiologies are conserved throughout the vertebrate evolution from fishes to humans.32 Indeed, about 71% of human genes have at least one ortholog in the zebrafish genome.23 On the other hand evolution has resulted in enormous diversity of life-forms in fishes via genetic adaptation to different habitats. This diversity is largely based on the whole genome duplication early in the teleost lineage and subsequent subfunctionalization, neofunctionalization and loss of genes, and reorganization of gene regulation.57 As a result, over 3100 human genes have at least 2 orthologues in the zebrafish genome and both species have several thousand unique genes without an ortholog in each other’s genome.23 Therefore, design of experiments and interpretation of the results cannot be based on the assumption that molecular entities and regulatory pathways behind the functions under study are always the same in zebrafish and humans. In order to draw correct conclusions from the zebrafish model to human cardiac electrophysiology, ion channel functions that are shared must be discriminated from those that are derived and novel in zebrafish and humans.7 The recent analysis of the zebrafish Kir2 channel composition provides a striking example how different the molecular basis of cardiac ionic current (I_{K1}) can be in zebrafish and human hearts.17 This finding warrants a careful examination of other cardiac ionic currents as well.44 This overview examines the current state of knowledge on the zebrafish cardiac ion channels with relation to the human cardiac ion channels.

Action potentials
Action potential (AP) of the zebrafish ventricle shares the main characteristics of the human cardiac AP. Most importantly the zebrafish ventricular AP has a long...
plateau phase, similar to the human cardiac AP, and consequently a distinct QT-interval in the electrocardiogram (Figs. 1 and 2).\textsuperscript{29,63} All phases (0-4) of the cardiac AP, with the exception of the rapid phase-1 repolarization, are present in the zebrafish heart (Fig. 1).\textsuperscript{40} The absence of the phase-1 repolarization suggests that the transient outward current ($I_{to}$) is tiny or absent in the zebrafish heart.\textsuperscript{2} Furthermore, it should be noted, that as an ectotherm the duration of cardiac AP in zebrafish varies with body temperature within its thermal tolerance range between 6.2°C and 41.7°C.\textsuperscript{34} In comparison to the hearts of endothermic vertebrates, ion channel function in ectothermic fishes is scaled down to lower temperatures. The duration of zebrafish ventricular AP at 19°C is similar to the human ventricular AP at 37°C, while at the human body temperature the duration of the zebrafish ventricular AP is only about one fifth of the duration of the human cardiac AP (Fig. 1).

Inward rectifier K$^+$ current ($I_{K1}$)

The cardiac inwardly rectifying K$^+$ current ($I_{K1}$) stabilizes the resting membrane potential (phase-4) and is responsible for shaping the initial depolarization and the final phase-3 repolarization of the cardiac AP.\textsuperscript{22} A robust background $I_{K1}$ is present in atrial and ventricular myocytes of the adult zebrafish, and similar to mammalian hearts, the density of $I_{K1}$ is markedly higher in ventricular than atrial myocytes.\textsuperscript{40} There is, however, remarkable differences in cardiac $I_{K1}$ channel composition between human and zebrafish hearts. The human cardiac $I_{K1}$ is produced by Kir2.1, Kir2.2 and Kir2.3 channels. Kir2.1 channel forms about 50% of the Kir2 transcripts in the right ventricle,\textsuperscript{14} while in the right atrium Kir2.3 is the main Kir2 isoform (56%) with less contributions by Kir2.2 (31%) and Kir2.1 (13%) channels.\textsuperscript{14} In the zebrafish heart 6 Kir2 channel isoforms are expressed at the transcript level. In the ventricle an ortholog to the mammalian Kir2.4 channel is the main Kir2 channel isoform constituting 92.9% of the total Kir2 population. In the zebrafish atrium, Kir2.2a and Kir2.4 form 64.7% and 29.3% of the Kir2 transcripts, respectively.\textsuperscript{17} Notably Kir2.1a, Kir2.1b and Kir2.3 together form less than 6% and 1% of the Kir2 transcripts in zebrafish atrium and ventricle, respectively. Thus, the

Figure 1. Ventricular action potential of the zebrafish heart. (A) Typical action potential of the zebrafish ventricle shows fast upstroke (phase-0), long plateau (phase-2), rapid repolarization (phase-3) and stable resting membrane potential (phase-4), but lacks the fast phase-1 repolarization (arrow), which is typical for the human cardiac action potential (top right). As an ectotherm action potential duration and heart rate in the zebrafish is temperature-dependent within the thermal-tolerance range of the species. (B) Representative microelectrode recordings of ventricular AP at selected temperatures (36°C, 28°C and 19°C) and (C) within the whole range of temperatures between 10°C and 36°C.
Kir2 composition of the zebrafish heart is dominated by an isoform, which in mammals is hardly expressed in cardiac myocytes.\textsuperscript{13,24,54}

There are also functional differences between zebrafish and mammalian Kir2 channels. The zebrafish Kir2.4 is about 2 orders of magnitude more sensitive to Ba\textsuperscript{2+} block than its mammalian counterpart. On the other hand zebrafish Kir2.1a is almost an order of magnitude less sensitive to Ba\textsuperscript{2+} block than the mammalian Kir2.1 channels.\textsuperscript{17}

Delayed rectifier K\textsuperscript{+} currents (I_{Kr}, I_{Ks})

The two major repolarizing K\textsuperscript{+} currents, that end the long plateau phase of the human cardiac AP, are I_{Kr} and I_{Ks}. They are active during the phases 2 and 3 of the cardiac AP. I_{Kr} is the main repolarizing current of the human heart, while I_{Ks} comes into a play when more repolarizing reserves are needed, e.g. under \(\beta\)-adrenergic activation and with increasing heart rates.\textsuperscript{50}

In the human heart the pore forming component of the I_{Kr} channel (human erg1 or herg) is encoded by the KCNH2 gene\textsuperscript{49,59} and the functional I_{Kr} channels are heterotetramers of the 2 splice variants of the KCNH2 gene, herg1a and herg1b.\textsuperscript{26} I_{Kr} is also the main repolarizing K\textsuperscript{+} current in atrial and ventricular myocytes of the zebrafish heart.\textsuperscript{40,60} Interestingly, in the zebrafish heart I_{Kr} is not produced by erg1 channels but by erg2 channels, which are encoded by the zebrafish ortholog to the mammalian KCNH6 gene.\textsuperscript{30}

Figure 2. Comparison of human and zebrafish electrocardiograms (ECG). (Top) ECG of an adult zebrafish at 23°C kindly provided by prof. Tzung Hsiai. (Bottom) ECG of a healthy 43-year old human male. For direct comparison of zebrafish and human ECGs both recordings are shown in the same time scale. Similar to the human electrocardiogram, P, QRS and T waves are clearly distinguishable in the zebrafish ECG.
0.15 and 99.4 ± 0.08% of the transcripts in atrium and ventricle, respectively) (Fig. 3). In mammals erg2 is expressed in the nervous tissue but not in the heart, while in zebrafish erg1 is very weakly expressed in the heart.30 Thus, the IKr is generated by non-orthologous genes in human (erg1) and zebrafish (erg2) hearts.

Biophysical properties of the human erg1 and the zebrafish erg2 also differ. Steady-state activation and inactivation of the zebrafish IKr are −15 mV and +23 mV, respectively, different from the respective values of the human IKr, when measured in the same cellular environment (Xenopus oocytes). Furthermore, the presence of herg1b splice variant in the channel assembly affects drug sensitivity of the human IKr.1,27,38 Mutations in the zebrafish erg channel cause similar electrophysiological features that are typical for short QT and long QT syndromes in humans.3,16 QT-prolonging drugs induce AP prolongation, bradycardia and atrioventricular conduction block in zebrafish embryos.28,39

Different from the human heart, there is no direct demonstration on the presence of IKs in the zebrafish cardiac myocytes.2,40 The mammalian cardiac IKs is generated by a heteromultimeric assembly of Kv7.1 (KCNQ1 gene) α-subunits and minK (KCNE1 gene) β-subunits. Although IKs has not been reported for zebrafish cardiac myocytes,2,40 transcripts of the zebrafish orthologues to the mammalian KCNQ1 and KCNE1 genes are expressed in the zebrafish heart.62 Experiments with another fish species (Carassius carassius) of the zebrafish family (Cyprinidae) suggest that, when present, the fish cardiac IKs is mainly produced by homotetramers of Kv7.1 channel without the MinK β-subunit and with distinctly different electrophysiological properties.20 Unlike the mammalian IKs, the fish cardiac IKs has fast activation kinetics, is independent of stimulation frequency, is not augmented by cAMP-dependent pathway and is less sensitive to chromanol 239B block than its mammalian counter-part.20 Similar to the human heart also other members

![Figure 3](image-url)
of the $K_{\alpha 7}$ channel subfamily ($KCNQ2-4$) are expressed to some extent in the zebrafish heart.\textsuperscript{35,62}

**Calcium currents**

$Ca^{2+}$ currents ($I_{Ca}$) maintain the long plateau phase of cardiac APs (phase-2) and provide activator $Ca^{2+}$ for contraction. Atrial and ventricular myocytes of the zebrafish heart have both T-type ($I_{CaT}$) and L-type ($I_{CaL}$) $Ca^{2+}$ currents,\textsuperscript{6,8,40,47} while in adult mammalian heart the presence of $I_{CaT}$ is mainly restricted to the sinoatrial node and the conductive pathways. Notably, the density of $I_{CaL}$ is markedly larger in zebrafish ventricular myocytes than in human cardiomyocytes.\textsuperscript{65}

In mammals, there are 4 alpha1 subunits of the L-type $Ca^{2+}$ channels ($\alpha 1S$, $\alpha 1C$, $\alpha 1D$, $\alpha 1F$, or $Ca_{1.1-4}$) $Ca_{1.2}$ being the dominant cardiac isoform.\textsuperscript{37} In the zebrafish heart ventricular contraction is abolished by mutation in the $\alpha$-1C subunit ($Ca_{1.2}$) strongly suggesting that $I_{Ca}$ is produced by orthologous genes in humans and zebrafish. In the heart of adult zebrafish transcripts of the $\alpha$-1D ($Ca_{1.3}$) are also expressed.\textsuperscript{52} $I_{CaT}$ is an important component of pacemaker and conductive tissues, but usually absent in atrial and ventricular muscle of adult mammals. In this respect zebrafish is clearly different from humans and other mammals. Two $\alpha$ subunits of T-type $Ca^{2+}$ channels ($Ca_{3.1}$ and $Ca_{3.2}$) are expressed in mammalian hearts.\textsuperscript{11,43} T-type channel composition of the zebrafish has not been studied, but Ni$^{2+}$ sensitivity suggests that it might be an ortholog to the mammalian $Ca_{3.1}$,\textsuperscript{40} while immunofluorescence findings suggest the presence of $Ca_{3.2}$.\textsuperscript{11} The diversity of $Ca^{2+}$ channel $\alpha$-subunits is, however, much higher in fishes than mammals due to the whole genome duplication in the teleost lineage. Indeed in fugu (Fugu rubribes) 21 $Ca^{2+}$ channel $\alpha$-subunits have been found and as many as 16 of them are expressed in the heart.\textsuperscript{61}

**Sodium currents**

The voltage-gated $Na^{+}$ channels have a central role in excitability of myocardial cells, because they generate the rapid upstroke of the myocardial AP (phase-0) and determine the velocity of impulse transmission over the heart.\textsuperscript{15,46} A fast $Na^{+}$ current ($I_{Na}$) exists in atrial and ventricular myocytes of the zebrafish heart.\textsuperscript{40,60} The rate of AP upstroke is slower in zebrafish atrial and ventricular muscle in comparison to human heart suggesting that $I_{Na}$ density is significantly lower in the zebrafish heart.\textsuperscript{40} In cultured cardiac myocytes of the zebrafish embryos, $I_{Na}$ current density is equal in atrial and ventricular myocytes, but the atrial $I_{Na}$ activates at slightly more negative voltages in comparison to the ventricular $I_{Na}$.\textsuperscript{60}

In larval cardiac tissue (72 hpf) of the zebrafish 2 $\alpha$-subunits of $Na^{+}$ channels (SCN5Laa and SCN5Lab), orthologous to the human cardiac SCN5A, are expressed.\textsuperscript{42} However, in the adult zebrafish heart only SCN5Lab has been found.\textsuperscript{9} In contrast to the mammalian cardiac $Na^{+}$ channel (SCN5A) the $Na^{+}$ channels of the fish heart are about 3 orders of magnitude more sensitive to tetrodotoxin (TTX).\textsuperscript{21} This is due to the replacement of non-aromatic cysteine (C401) in the poor loop of the domain-I with an aromatic tyrosine (Y401) in the fish cardiac $Na^{+}$ channels. Since this replacement is also present in both paralogs of the zebrafish cardiac $Na^{+}$ channel, the zebrafish $I_{Na}$ is also highly sensitive to TTX.\textsuperscript{9,40,58} Association of the zebrafish SCN5Lab with its beta1-subunit increases $I_{Na}$ amplitude when expressed in the CHO cell line.\textsuperscript{10} Collectively these findings suggest that the paralogs of the zebrafish cardiac $Na^{+}$ channels are orthologous to the main human cardiac isoform, but different from the mammalian $I_{Na}$ the zebrafish $I_{Na}$ is TTX-sensitive.

**Other ionic currents**

Practically nothing is known about the ligand-gated inward rectifiers currents, the ATP-sensitive $K^{+}$ current ($I_{KATP}$) and the acetylcholine-activated $K^{+}$ current ($I_{KACH}$) of the zebrafish heart. $I_{KATP}$ has been recorded from cardiomyocytes of some fish species and therefore it is likely that similar current exists also in zebrafish cardiac myocytes. Three ATP-sensitive channels have been found in the zebrafish genome (Kir6.1, Kir6.2 and Kir6.3) located in different chromosomes.\textsuperscript{54} Synteny data suggests, however, that the Kir6.3 is in fact a paralogue of the Kir6.2 (i.e. Kir6.2b) (Table 1). In mammals the conductance pore of ATP-sensitive channels is produced by Kir6.1 and Kir6.2 channels, which assemble with sulfonylurea receptors to produce fully functional channels. No data is available on the expression of these channels in the zebrafish heart. In the goldfish (Carassius auratus) heart Kir6.1 and Kir6.2 channels are expressed.

Acetylcholine induces a large inwardly rectifying $K^{+}$ current in atrial but not in ventricular myocytes of
the zebrafish heart. However, the molecular basis of this current has not yet been resolved.

Pacemaker current (I_P or I_h) has been demonstrated to be present in cultured cardiac myocytes of embryonic zebrafish as well as in cultured atrial and ventricular myocytes of the adult zebrafish. Down-regulation of the I_h by a recessive slo mo mutation (which probably encodes a mitochondrial protein) causes depression of intrinsic heart rate, especially in the embryonic heart. The zebrafish I_h consist of slow and fast components suggesting that it is produced by 2 different channels similar to the human heart. Pacemaker tissue of the zebrafish heart demonstrates the presence of HCN4 channels as one of the likely candidates for coding the I_h channels.

Conclusions and implications

Considering the increasing use of zebrafish as a model for human cardiac electrophysiology, cardiac arrhythmias and drug screening, our knowledge on the zebrafish cardiac ion channels, their biophysical properties, drug sensitivity, molecular basis and regulatory networks is still limited. The current knowledge indicates that human and zebrafish myocytes share several electrical properties, but on the other hand several differences also exist between human and zebrafish cardiac APs, ion channel function and ion channel molecular composition (Table 2). Zebrafish and human hearts both have a distinct plateau phase. In this respect the zebrafish heart is clearly a better model than the murine heart, which is characterized by a short AP plateau and strong reliance on I_To in AP repolarization. Theionic current basis of human and zebrafish cardiac APs is similar in that I_K1 and I_Ks are the major repolarizing currents in both hearts. On the other hand, zebrafish ventricular AP, unlike human cardiac AP, does not have clear phase-1 repolarization suggesting that the transient outward current (I_To) is not expressed in the zebrafish heart. Unlike human heart, atrial and ventricular myocytes of the zebrafish heart have both I_CaT and I_CaL. I_K1 and I_Kr are generated by different gene products in humans and zebrafish, and I_Ks may be absent from the zebrafish heart.

A number of excellent techniques have been developed for recording electrical and mechanical activity of the zebrafish heart in vivo and in vitro, thereby making this small fish amenable for cardiac studies. Effects of disease causing mutations and pharmaceutical drugs on electrical excitation, rhythm and contraction of the zebrafish heart can be traced with high accuracy, making it putatively an interesting model for human cardiac electrophysiology. Due to the presence of ion channel paralogues in the zebrafish

### Table 1. The current state of knowledge about the ionic currents and ion channels of the zebrafish heart.

| Current | Protein (α-subunit) | Gene | References |
|---------|---------------------|------|------------|
| I_Na   | Na_1.5a, Na_1.5b    | SCNSLAa, SCNSLAb | 10,60 |
| I_CaL  | Ca_2.1a Ca_2.1b     | CACNA1C CACNA1D | 8,40,47,65 |
| I_CaT  | Ca_2.3, Ca_2.2      | CACNA2B CACNA1H | 5,40 |
| I_K1   | K_1,1.2 (Erg3) K_1,1.1 (Erg1) K_1,1.1 (Erg1) K_1,1.1 (Erg1) | KCNH6 KCNH2A KCNH2B KCNH4 | 62 |
| I_K7.1 | K_7.1               | KCNJ1 QCN1 | 17,40 |
| I_K1   | Kir2.4 Kir2.2a      | KCNJ14 KCNJ12A KCNJ12B KCNJ2A KCNJ2B KCNJ4 | 5,40,60,64 |
| I_KATP | Kir2.1a Kir2.1b     | NK KCNJ8 KCNJ11A KCNJ11B | 63 |
| I_If   | Kir6.1               | | |
| I_KaCh | Kir6.2a              | | |
| I_Km   | Kir6.2b Kir6.2a      | | |

* I_Km current has not been found in the zebrafish heart; **I_KATP current has not been measured in the zebrafish heart; NK, not known

### Table 2. Similarities and differences of the zebrafish cardiac electrophysiology with the human cardiac electrophysiology.

| Similarities with human cardiac electrophysiology | Differences to human cardiac electrophysiology |
|---------------------------------------------------|-----------------------------------------------|
| Cardiac AP has a clear plateau phase. A distinct QT interval in ECG | Absence of the phase 1 repolarization (I_To not expressed) |
| Similar fundamental current systems (I_h, I_CaL, I_K) are present in atrial and ventricular myocytes. I_h and I_K1 are the main repolarizing currents. | The slow component of the delayed rectifier I_K is not expressed in the zebrafish heart. Large I_CaT is present in zebrafish atrial and ventricular myocytes. |

I_K1 is mainly generated by Kir2.4 and Kir2.2a channels. I_Kp is mainly generated by erg2 (KCNH6) channels. The balance of inward currents: density of I_Na low and density of I_Ca high in comparison to the human heart.
genome, differences in ion channel proteins and subunit composition of ion channels between zebrafish and human hearts, zebrafish is unlikely to be a good general-purpose model for the human cardiac electrophysiology. However, similarity of the major repolarizing ($I_{K_1}$, $I_{K_2}$) and depolarizing ($I_{Na}$, $I_{Ca_L}$) currents, despite of their partially different molecular basis, makes the zebrafish heart an appropriate model for more specific issues of human cardiac excitation. Because various Kir2 channels and different erg channels are mutually similar in function, i.e., all Kir2 channels are strong inward rectifiers and all erg channels show fast inactivation, fast recovery from inactivation and slow deactivation, species-specific differences in channel compositions may not be critical, when studying disease causing mutations or using functional knock-downs and knock-outs. The same applies to the inward currents, $I_{Na}$ and $I_{Ca_L}$. However, a prerequisite for these studies is that the ion channel composition of the zebrafish heart under study is known and correct channel paralogs and isoforms are targeted.

The special characteristics of the zebrafish cardiac ionic currents are more problematic in drug screening since different ionic currents, even if qualitatively similar to human counterparts, may show significant quantitative differences in drug affinity due to their different molecular basis. Another factor that complicates the use of zebrafish model in selection of candidate molecules for medicinal drug development or in toxicological testing is the total composition of inward and outward currents underlying the cardiac AP, which differs qualitatively (e.g, absence of $I_{T_{K_0}}$ and $I_{K_0}$) and quantitatively ($I_{Na}$, $I_{Ca_L}$) from that of the human heart. In risk/benefit assessment of new drug molecules, more emphasis is currently placed on the potential proarrhythmic effects of pharmaceuticals. According to the current research paradigm of safety pharmacology, proarrhythmic potential of the drugs should be look at the level of multiple ion channels ($I_{K_1}$, $I_{Ca_L}$, $I_{Na}$, $I_{K_2}$ and $I_{T_{K_0}}$) instead of one particular ion channel, since drug molecules may bind to several targets. In this experimental approach the total repolarizing reserve of outward currents and the total depolarizing reserves of inward currents is considered decisive in estimating the proarrhythmic liability of pharmaceuticals. Because of the qualitative and quantitative differences in inward and outward currents between zebrafish and human hearts, zebrafish heart and cardiac myocytes are likely to pose problems in nonclinical safety pharmacology and toxicology, especially in regard to arrhythmia liability of drugs.

Clearly, more research on molecular basis of cardiac ion channels, and ion channel regulation and drug sensitivity of cardiac ionic currents are needed to enable rational use of the zebrafish heart as an electrophysiological model for the human heart.

**Methods**

**Animals**

Zebrafish were reared at +28°C. All experiments were authorized by the National Animal Experimental Board in Finland (permission ESAV1/2832/04.10.07/2015).

**Action potentials**

Ventricular APs of spontaneously beating hearts were recorded with microelectrodes filled with 3M KCl (resistance about 20 mega ohms) in oxygenated external saline solution containing (in mM) NaCl 150, KCl 3.0, MgSO4 1.2, NaH2PO4 1.2, CaCl2 2.0, glucose 10.0 and HEPES 10.0 (at pH 7.7). Temperature of the tissue bath was changed at the rate of 3 degrees 10 min⁻¹.

**KCNH transcript expression**

Atrium and ventricle of the heart were separately snap frozen in liquid nitrogen. Tissues from 5 fishes were pooled for each atrial and ventricular sample (n = 6) and stored at −80°C. RNA was extracted by TriReagent (Thermo Scientific) and treated with RNase free DNase to avoid DNA-contamination. First-strand cDNA and -RT-control (reaction containing all other components except the RT-enzyme) were synthesized from each sample using Maxima H Minus First Strand cDNA Synthesis Kit (Thermo Scientific). Each sample was amplified in triplicates using Maxima SYBR Green qPCR Master Mix (Thermo Scientific) (Table 3) and AriaMx Real Time PCR System (Agilent Technologies) under the cycling parameters: 95°C for 10 min followed by 40 cycles at 94°C for 10 s, 60°C for 20 s and 72°C for 30 s, then 72°C for 5 min. Specificity of amplification was monitored by melting curve analysis from 65°C to 95°C. Transcript levels of KCNH genes were normalized to the expression of DnaJA2 reference gene.
Table 3. Primers used in qPCR.

| Gene | Primers (5’-3’) | Amplicon length (bp) |
|------|-----------------|----------------------|
| KCNH2A (ENSDARG000000029881) | F: TCTGTGATGTTGACTGCTC R: CTGAGAGTGCAGGACAGGAG | 100 |
| KCNH2B (ENSDARG000000060053) | F: GGATCTGCCCTGTGACCTGAC R: TTGAGAGTGCAGGACAGGAG | 102 |
| KCNH6 (ENSDARG00000001803) | F: ATTGCTGGCGGTGCTGACTG | 100 |
| KCNH7 (ENSDARG000000062687) | F: CTTCACACACTGCCAGGAA R: TGAGGTTGACAGGACAGGAG | 100 |

Abbreviations
AP action potential
hpf hours post fertilization
TTX tetrodotoxin

Disclosure of potential conflicts of interest
No potential conflicts of interest were disclosed.

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