Response to Numann and Gibson

We thank Drs Numann and Gibson for their interest in our work. They cite data that the sea anemone toxin ATXII does not affect Nav1.8 gating in dorsal root ganglion neurons and so raise the question of whether ATXII affects Nav1.8-mediated late current in heart cells. In experiments not presented in the article, we assessed the effect of ATXII on late current measured at the end of a 100-ms depolarizing pulse to +20 mV in SCN10A-transfected ND7/23 cells. With ATXII (100 nmol/L) exposure, the late current was increased ≈6 fold, from 241 pA at baseline to 1320 pA; ATXII-augmented current was 57% blocked by 10 nmol/L A803467 and 97% blocked by 100 nmol/L A803467. Furthermore, Figure 7 in the article strongly supports the idea that the effects of ATXII in mouse and rabbit cardiomyocytes are attributable, at least in part, to augmentation of Nav1.8-mediated current. Thus, our data along with reports such as those from Wu et al cited by Numann and Gibson, argue that ATX-II can be used to induce late sodium current and is antiarrhythmic. We would agree that like other pharmacological probes, the extent to which ATXII completely mimics pathophysiology is not established and that it would be of interest to examine the extent to which many gene products, studied in animal models, mediate ionic currents in human cardiomyocytes. We also agree that our data suggest that the evaluation of drugs developed to target Nav1.8 in dorsal root ganglion should include assessment of their effects on cardiac electric behavior.

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Disclosures

None.

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References

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