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Electrophysiological and trafficking defects of the SCN5A T353I mutation in Brugada syndrome are rescued by alpha-allocryptopine

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Brugada syndrome (BrS), which causes arrhythmias that lead to sudden cardiac death, is linked to loss-of-function mutations that affect sodium channels. Here, we investigate the rescue effect of alpha-allocryptopine (All) from Chinese herbal medicine in a T353I mutation of SCN5A, which combines trafficking abnormalities with Brugada syndrome. SCN5A-T353I expressed in HEK293 cells showed a small peak current (I_{peak}) of only 59.6% of WT and an observably sustained current (I_{sus}). We found that after treatment with All by direct perfusion for 5 min, neither WT nor T353I currents markedly changed. However, after incubating with All for 24 h, I_{peak} of the T353I in HEK293 cells was strongly enhanced. Furthermore, the enhanced plasma membrane (PM) expression of Nav1.5 was detected, indicating the rescued defective trafficking. Interestingly, the I_{sus} of T353I was significantly inhibited by All, which reduces the occurrence of LQT syndrome 3 (LQT3). We provide evidence that All can rescue the trafficking deficiencies and restore the cellular electrophysiological characteristics of SCN5A-T353I. This feature of All may benefit patients with the BrS-associated Nav1.5 channel and might have other potential therapeutic effects.

Biography

Yang Li has completed his PhD and postdoctoral studies from Tongji Medical College of HUST. He is expert of National Natural Science Foundation of China, committee member of China Medicinal Biotechnology Association, and the standing board or special reviewers of 10 journals. He has published more than 26 papers as first or Corresponding author.

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