Title: LSTM Based Autoencoder Model for Cardiac Activity Translation

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Abstract

Recent innovation and development of technologies in precision medicine promise more precise prediction of patient-specific identification of cardiac arrythmia vulnerability. Human pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) constitute a powerful invitro tool for preclinical assessment of cardiac safety liabilities and a step toward precision medicine. Combining iPSC-CMs for predicting patient-specific response to therapies with data-analytics techniques to map changes within the cardiac activity of iPSC-CMs to altered function in mature cardiomyocytes, may improve monitoring techniques for preclinical cardiac safety assessment. Recently, deep learning techniques have been widely used to advance personalized medicine. We took advantage of the long-short-term-memory (LSTM) autoencoder network in analyzing sequence data to translate cardiac activity from iPSC-CMs to mature cardiomyocytes. We used cardiac action potential (AP) traces from iPSC-CMs and mature cardiomyocytes generated by computational models to train a deep leaning network, which can then be used to translate from iPSC-CM APs to mature cardiomyocytes AP. We also trained the translator on virtual AP traces that had been subject to block of the rapidly activating delayed rectifier potassium channels (Ik_r). We have tested the accuracy of our translator with a distinct set of test data comprising APs and show that it can precisely translate a previously unknown dataset from iPSC-CM APs to accurately predict effects of hERG block on mature APs. Here we show that a deep learning network can be trained to translate between immature and mature cell action potential in the control setting and after perturbation by Ik_r block. Therefore, we can track the sensitivity and specificity of iPSC-CMs cardiac activity parameters and evaluate their influences on their corresponding values for mature cardiomyocytes. The translator can be applied to simulated or experimental data to improve our understanding of personalized cardiac safety liabilities.