ABSTRACT

In vitro differentiated cardiomyocytes as a Model for Triggered Arrhythmias

Ying Ming Zhang and Sam Dudley

Atlanta VA Medical Center and Department of Medicine, Emory University

INTRODUCTION

Many cardiac arrhythmias are associated with afterdepolarizations that are caused by the unbalancing of inward and outward currents. Unbalancing may be associated with changes in intracellular and extracellular concentrations of ions, or with changes in the characteristics of ionic currents. Changes in the ratio of inward to outward currents may lead to oscillations in the membrane potential because of an imbalance between voltage-dependent repolarizing and depolarizing currents during phase 2 or 3 of the AP. These afterdepolarizations may be caused by a variety of factors, including digitalis intoxication, increased Na/Ca exchange, or by manipulation such as changing the Ca concentration ([Ca2+]o). In this study, we demonstrate that different cardiomyocytes that differ in their physiological properties can exhibit different afterdepolarizations.

Dissociated cardiomyocytes should allow for rapid phenotyping screening of genetic changes such as new agents or mutations associated with human arrhythmias. In the study, we screen a new drug that different cardiomyocytes that differ in their physiological properties can exhibit different afterdepolarizations.

METHODS

In vitro differentiated cardiomyocytes from ESCs and ECCs are generated by culturing embryoid bodies (EBs) in suspension. EBs are cultivated in suspension for 7-12 days, and then allowed to differentiate into cardiomyocytes. The differentiated cardiomyocytes are then perfused with solutions containing 20 mM TEA. The perfused cardiomyocytes are then studied in the whole cell patch clamp mode and perfused with solutions containing 20 mM TEA. The perfused cardiomyocytes are then studied in the whole cell patch clamp mode and perfused with solutions containing 20 mM TEA. The perfused cardiomyocytes are then studied in the whole cell patch clamp mode and perfused with solutions containing 20 mM TEA.