Treating Cancer-Drug-Induced Contractile Dysfunction With The Polyamine Spermidine

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BACKGROUND

Doxorubicin (DOX) is a cancer drug used to treat childhood and adult malignancies, including pediatric leukemia and breast cancer. However, despite being a cornerstone for oncological care, the use of DOX is limited by dose-dependent cardiotoxicity, which can lead to contractile dysfunction and heart failure. Yet, DOX is still widely used due to the lack of suitable replacements. Sarcomere degradation and impairment of autophagy are thought to be the mechanisms that cause DOX-induced cardiotoxicity. With a higher incidence of cancer drug-induced cardiotoxicity in our aging population, there is a great need for therapies that can reverse the toxic effects of chemotherapies. Furthermore, overcoming this cardiotoxicity would tremendously aid clinicians in treating patients with a variety of cancers by allowing for a more aggressive therapeutic response to the disease.

DESCRIPTION

Researchers at the University of California, Santa Barbara have leveraged spermidine, a natural polyamine that plays a vital role in cellular functions, to ameliorate the cardiotoxic effects of cancer drugs including doxorubicin (DOX). Micromolar concentrations of spermidine are sufficient to elicit an increase in the contractile function of human-induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) which demonstrated a reduction in contractile function when exposed to DOX. These results suggest that spermidine, perhaps acting as an autophagy activator, can enhance contractile force post-DOX treatment, increase the hiPSC-CMs size, and support a more robust and organized sarcomere network. This invention provides a path for developing further therapies that target autophagy and sarcomere proteostasis to treat cardiac dysfunction.

ADVANTAGES

▶ Reverses and ameliorates the cardiotoxic effects of cancer compounds like doxorubicin
▶ Offers new path for discovering treatments for cardiac dysfunction

APPLICATIONS

▶ Therapeutics
▶ Drug discovery
▶ Medical Food/Nutraceuticals

RELATED MATERIALS
Abstract 14213: The Polyamine Spermidine Enhances the Contractile Force of µ-Patterned Single-Cell Stem-Cell-Derived Cardiomyocytes Post Doxorubicin Treatment - 10/30/2022

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Wafer-Scale Protein Patterning Of Hydrogel Devices
- Hydrogel Surface With Anatomically Accurate Anisotropic Nanometer-Scale Topography