INTRODUCTION

Aging light chain (LC) light chains is a common, progressive, and typically fatal disorder caused by aberrant production of fibrillar LC. Fibrillization of LC results in the formation of insoluble amyloid deposits that lead to tissue dysfunction.

- An excess of LCs prior to binding is produced by prostate cancer cells.
- Accumulation of LC has been linked to the heart, brain, and skin, resulting in significant organ dysfunction.

Early detection of amyloidosis in patients with AL, amyloidosis, particularly those with cardiac involvement, is challenging. In patients with AL disease, the median time from diagnosis to death is only 3.5 years. Therefore, there is a critical need for early detection and monitoring of disease progression.

Neonatal rat hearts were freshly dissociated and cultured using the primary cardiomyocyte isolation kit according to the manufacturer’s instructions (Thermo Scientific Pierce). Briefly, after 5 days in culture, cardiomyocytes were serum starved overnight and treated with Dulbecco-modified Eagle medium (DMEM) alone (vehicle control), 10 nM endothelin-1 (ET-1) and/or the small molecule inhibitors tin protoporphyrin IX (heme oxygenase-1 [Hmox-1] inhibitor [Hmox-1i]) at 30 µM for 6 hours. A LC was detected using a method by Wall et al.17 Cell surface–bound LC aggregates and cardiac hypertrophy result in early markers of oxidative stress response, such as Egr-1 (early growth response) protein expression and intracellular H2O2 levels.

RESULTS

LC Aggregates Induced Cellular Stress in Cardiomyocytes

Intracellular ROS levels, Egr-1 transcriptional response, and NT-proBNP secretion into conditioned media in response to treatment with FL-λ6A were measured by quantitative polymerase chain reaction (qPCR) and ELISA, respectively. NT-proBNP secretion was found to be a standard index of the tissue. Results generated from a pilot study demonstrated that Egr-1 and Hmox-1 expression levels were significantly increased in response to LC treatment.

These results further support the concept that LC aggregates and cardiac hypertrophy activate distinct intracellular signaling pathways in cardiomyocytes. These results are consistent with the model whereby LC aggregates and cardiac hypertrophy activate distinct intracellular signaling pathways in cardiomyocytes. These results are consistent with the model whereby LC aggregates and cardiac hypertrophy activate distinct intracellular signaling pathways in cardiomyocytes. These results are consistent with the model whereby LC aggregates and cardiac hypertrophy activate distinct intracellular signaling pathways in cardiomyocytes.

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