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SurR9C84A exhibits cardioprotective effects against melphalan induced cardiotoxicity in primary human cardiomyocytes

Ajay Ashok, Jagat R Kanwar and **Rupinder K Kanwar**
Deakin University School of Medicine, Australia

Cancer chemotherapy leads to cardiac toxicity and adverse cardiac muscle injury. Novel therapeutics that salvage cardiac damage (apoptosis) and revive affected cardiomyocytes are urgently required. Survivin, an inhibitor of apoptosis is a bifunctional protein with a role in cell proliferation. We have recently reported the neuroprotective properties of SurR9C84A which is a cell-permeable dominant negative mutant recombinant survivin protein. The cardioprotective nature of SurR9C84A against melphalan induced cardiotoxicity in primary human cardiomyocytes (HCM) was investigated in this study. We hypothesized that SurR9C84A would be a potent cardioprotective agent against melphalan induced cardiotoxicity, by inhibiting cell apoptosis and inducing cell proliferation. The dose of melphalan was optimized to induce cardiotoxicity in HCM and the cardioprotective effects were studied after 4 days of SurR9C84A treatment. Cell proliferation and apoptosis were detected by CyQUANT and Annexin-V kits, respectively. The changes in expression of cardiac damage markers; free cardiac troponin T, creatine kinase and other vital anti-stress proteins were analyzed by immunoblotting. Melphalan treatment induced 40% toxicity in HCM. Cellular uptake of SurR9C84A increased proliferation of HCM, upregulated survivin and proliferating cell nuclear antigen expression, inhibited apoptosis and caused actin regeneration in the damaged HCM. A significant downregulation of f cTnT, creatine kinase, matrix metalloproteinase-9, angiotensin 2 receptor, Bax, interleukin-1β, cytochrome C and caspase-3 was observed. SurR9C84A was nontoxic to normal HCM. In conclusion, our study identifies the cardioprotective nature of bifunctional SurR9C84A in HCM regeneration and its future implications in designing protein therapeutics to relieve the effects of anti-cancer drugs on heart.

Biography

Ajay Ashok has completed his Bachelor in Technology (Biotechnology) from SRM University and Masters in Technology from SASTRA University (School of Medical Nanotechnology) with the highest grade awarded for the degree. He is currently pursuing his PhD at Deakin University, School of Medicine, Australia. Due to his merits, he was awarded The Deakin University Post graduate International Research Scholarship for a PhD course in 2012. He had previously presented his other studies at various other reputed conferences such as the World Congress of Cardiology in 2014 and International Nanomedicine Conference, Sydney 2012.

aasho@deakin.edu.au