ERYTHROPOIETIN DELIVERED FOR KIDNEY PROTECTION MAY HAVE SECONDARY BENEFITS IN PROTECTING HEART

Christudas Morais[1], David A Vesey[1,2], David W Johnson[1,2], Glenda C Gobe[1]

[1]Centre for Kidney Disease Research, School of Medicine, Translational Research Institute, University of Queensland and [2]Dept Renal Medicine, Princess Alexandra Hospital, Brisbane, Australia

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

INTRODUCTION

Acute kidney injury (AKI) is a common complication in hospitalized patients, especially those in the intensive care units. AKI and renal failure can lead to heart complications and concurrent worsening of structure and function in both organs. Recombinant human erythropoietin (rhEPO) has been found to have protective functional and structural outcomes in both experimental animals and humans with AKI (1, 2), but it is not known if treatment of the AKI with rhEPO also protects any concurrent injury to the heart. The aim of this study was to use isoproterenol (ISO) on cardiac cells in vitro as a model to mimic heart failure (3), to test whether rhEPO modulates the outcome.

AIM

To investigate the role of rhEPO in ISO-induced cardiac injury or repair response of H9c2 rat cardiomyoblasts.

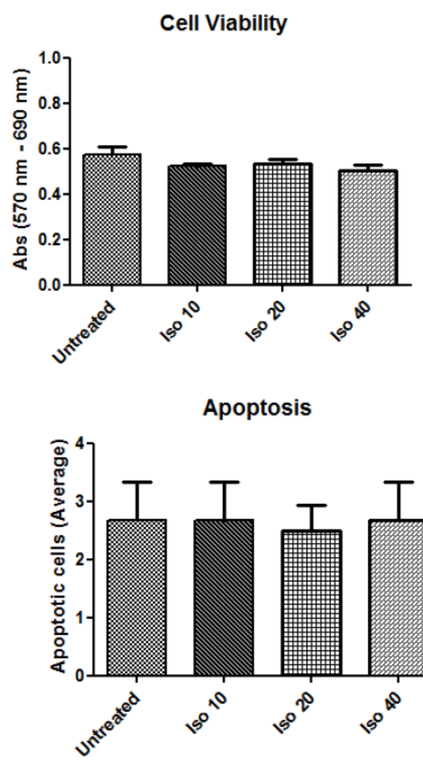
METHODS

- H9c2 cardiomyoblasts were seeded in 96-well plates, or on glass coverslips in 24-well plates
- The cells were treated with ISO (10, 20 and 40μM) or rhEPO (50, 100 or 200IU) or a combination of both
- The compounds were dissolved in culture medium.
- In the combination group, rhEPO was added 60 seconds after the ISO treatment.
- Untreated and placebo (for rhEPO) treated groups served as controls.
- Forty-eight hours after treatment, cell viability was measured by MTT assay.
- The cells grown on coverslips were stained with haematoxylin and eosin (H&E) and analysed for proliferation and apoptosis.
- H&E stained cells were photographed with a Nikon Eclipse microscope and hypertrophy was measured using NIS/Elements software.

RESULTS

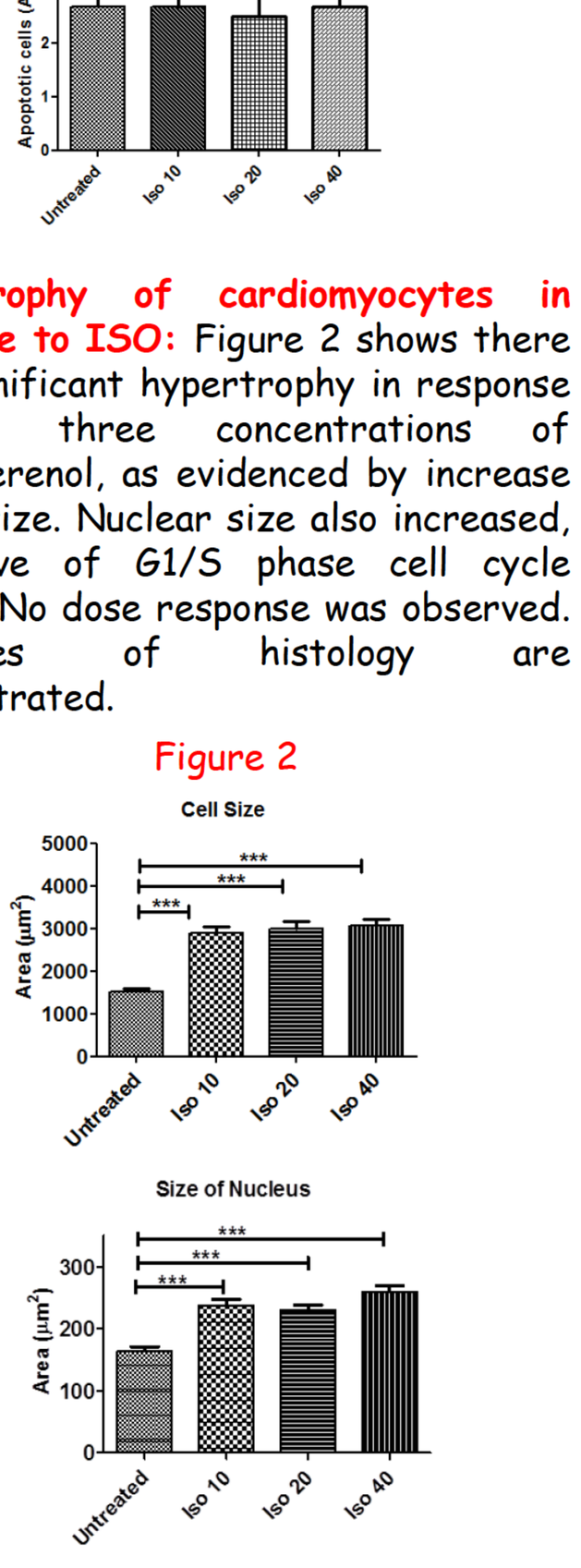
Cell death and Apoptosis: The compounds, either alone or in combination, did not induce any significant changes in cell viability or apoptosis (Figure 1, next column, top).

Figure 1



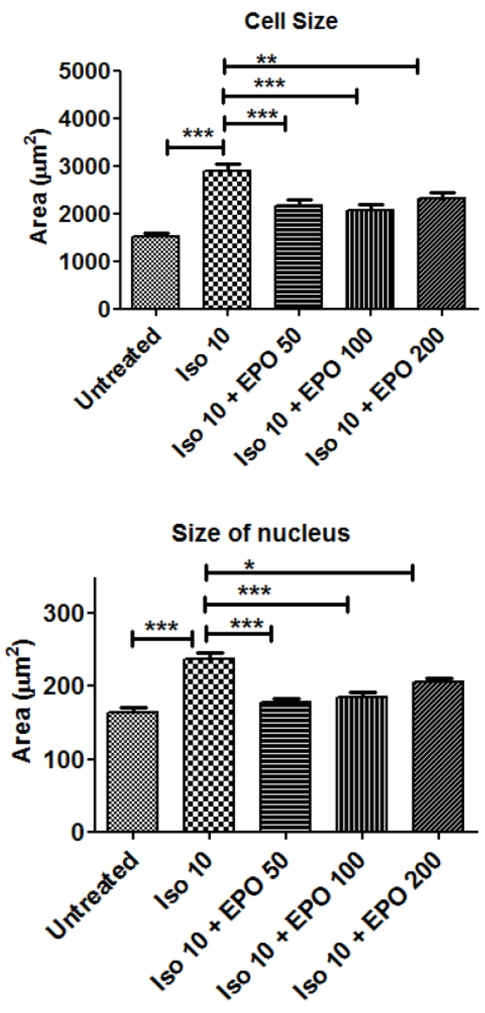
Hypertrophy of cardiomyocytes in response to ISO: Figure 2 shows there was significant hypertrophy in response to all three concentrations of isoproterenol, as evidenced by increase in cell size. Nuclear size also increased, indicative of G1/S phase cell cycle arrest. No dose response was observed. Examples of histology are demonstrated.

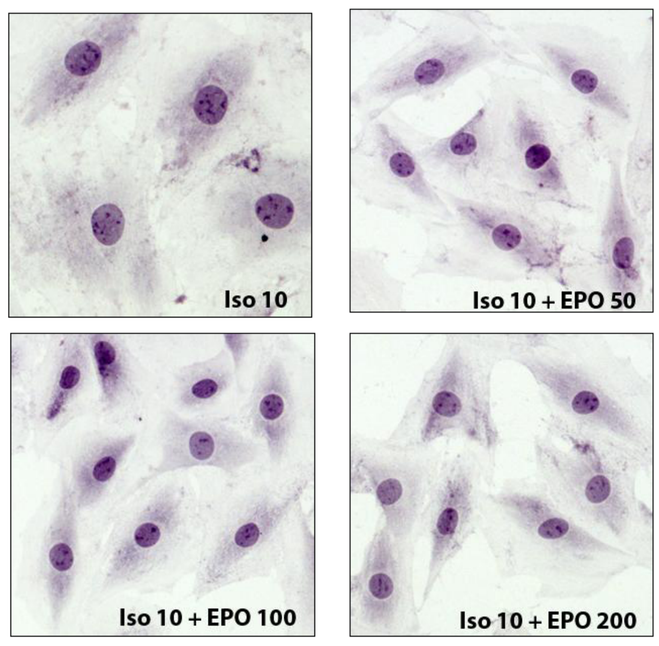
Figure 2



EPO attenuates isoproterenol-induced hypertrophy: All concentrations of EPO (50, 100 and 200 IU) significantly decreased the isoproterenol-induced hypertrophy, however, no dose response was observed (Figure 3).

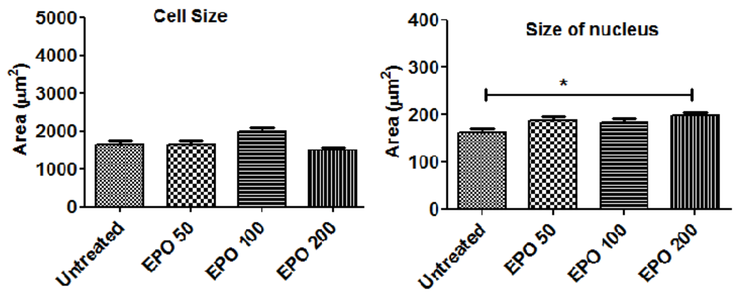
Figure 3





By itself, none of the three concentrations of EPO induced any significant changes in cell size. However, 200 IU of EPO induced a slight but significant increase in the size of nucleus (Figure 4).

Figure 4



SUMMARY AND CONCLUSIONS

If rhEPO is used to protect the kidneys in AKI, it may have secondary beneficial effects in protecting the heart cells from hypertrophy, thought to be a maladaptive response to injury as part of AKI-induced cardiorenal syndrome.

References

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Acknowledgement
Funding by NHMRC

DOI: 10.3252/pso.eu.50era.2013