

Genetically Engineered Mouse Embryonic Stem Cell – derived Cardiomyocytes as a Suitable Model on Drugs Toxicity In vitro

*Leila Dehghani^{1,2}, Mohammad- Hossein Nasr Esfahani², Soheil Tahani^{1,3}

¹ Isfahan Neurosciences Research Centre, Isfahan University of Medical Sciences, Isfahan, Iran.

² Department of Cell and Molecular Biology, Cell Science Research Center, Royan Institute for Animal Biotechnology, (ACECR), Isfahan, Iran.

³ Department of Medical Sciences, Islamic Azad University, Najafabad Branch, Isfahan, Iran.

Background

DOX is a powerful chemotherapeutic agent used in the treatment of solid tumors and malignant hematological diseases. However, its cardiac toxicity limits the clinical usefulness of this drug. Previous reports have shown Corticosteroids induce a cytoprotective effect on cardiomyocytes. Mouse transgenic embryonic stem cell-derived pure cardiomyocytes may be considered as a model for assessment pharmacological and toxicological effects of drugs in vitro.

Methods

Mouse transgenic embryonic stem cell-derived pure cardiomyocytes were treated by different concentrations of doxorubicin to determine DOX LD50. Pure cardiomyocytes were evaluated in two groups: treatment by 10 μ M DEX 24 h before or before and in continuation with DOX. The percentage of cardiomyocyte viability by MTS assay, the percentage of beating and quantitative Real Time polymerase chain reaction (Real Time-PCR) for cardiac gene expression (β -MHC) was evaluated in each group.

Results

5 μ M DOX was determined as drug concentration that leads to 50% cardiomyocyte mortality. Cardiotoxicity on mouse transgenic embryonic stem cell-derived pure cardiomyocytes can be ameliorated by treatment with dexamethasone (DEX) when DEX administrated before DOX. The effect of DEX appears to be mediated via glucocorticoid receptors. DEX increases cardiomyocyte gene expression and decreases apoptosis.

Conclusion

Transgenic embryonic stem cell derived cardiomyocytes are a model for evaluation of doxorubicin toxicity. Additionally, this model provides us with a clinical suggestion, which proposes that the beneficial effect of DEX is obtained when DEX was added only before DOX. Also the results of present study were consistent with in vivo result in mice.

Key words: Apoptosis, Cardiotoxicity, Doxorubicin, Mouse Transgenic Embryonic Stem Cell.

Poster Presentation

***Corresponding Author:** Leila Dehghani, Department of Cell and Molecular Biology, Cell Science Research Center, Royan Institute for Animal Biotechnology, (ACECR), Isfahan, Iran.