



## Strathprints Institutional Repository

**Laovitthayangoon, Sarunya and Tate, Rothwelle and Currie, Susan and Grant, Mary Helen (2016) Cobalt cardiotoxicity - effects on the contractile and non-contractile cells of the heart. FASEB Journal, 30 (1). ISSN 0892-6638 ,**

This version is available at <http://strathprints.strath.ac.uk/57179/>

**Strathprints** is designed to allow users to access the research output of the University of Strathclyde. Unless otherwise explicitly stated on the manuscript, Copyright © and Moral Rights for the papers on this site are retained by the individual authors and/or other copyright owners. Please check the manuscript for details of any other licences that may have been applied. You may not engage in further distribution of the material for any profitmaking activities or any commercial gain. You may freely distribute both the url (<http://strathprints.strath.ac.uk/>) and the content of this paper for research or private study, educational, or not-for-profit purposes without prior permission or charge.

Any correspondence concerning this service should be sent to Strathprints administrator: [strathprints@strath.ac.uk](mailto:strathprints@strath.ac.uk)

## **Cobalt cardiotoxicity - effects on the contractile and non-contractile cells of the heart**

Laovithayangoon, S., Tate, R., Currie, S. & Grant, M. H. 30 Apr 2016 In : FASEB Journal. 30, 1, 178.7

### **[EB2016 Experimental Biology Meeting 2016](#)**

Exposure to cobalt is known to cause cardiotoxicity and a common source of cobalt exposure is from metal-on-metal bearings used in prosthetic joint replacements. Acute and chronic effects of cobalt at a cellular level in the heart are not well understood. This study investigated the effects of cobalt (CoCl<sub>2</sub>) treatment on contractile and non-contractile cells of the heart. We have used isolated adult rat ventricular papillary muscles to investigate the effects of CoCl<sub>2</sub> on basal and isoprenaline-stimulated contractile responses. In addition, we used freshly isolated primary adult rat ventricular fibroblasts maintained in short-term culture to assess the effects of CoCl<sub>2</sub> on cell viability and proliferation. Stimulation of isolated ventricular papillary muscles with the positive inotrope isoprenaline (1 $\mu$ M) resulted in a consistent increase (~35% increase) over the basal contractile response as expected. Following treatment with CoCl<sub>2</sub> (1 $\mu$ M) for 4h, there was a dramatic reduction in both the basal and isoprenaline-stimulated contractile responses (both~40% reduction). This effect was not due to a time-dependent decrease in contractility since in separate parallel control preparations consistent increases in contraction were observed following 1 $\mu$ M isoprenaline challenges at time zero and after 4h without CoCl<sub>2</sub>. Examination of the effects of CoCl<sub>2</sub> on cardiac fibroblast proliferation and viability was performed using a range of assays. To assess effects on proliferation, MTT, neutral red and crystal violet assays were all used to compare effects of increasing concentrations of CoCl<sub>2</sub> on the Swiss 3T3 fibroblast cell line and primary cardiac fibroblasts. Over 72h, increasing CoCl<sub>2</sub> concentrations (up to 500 $\mu$ M) resulted in decreased proliferation. The MTT and Crystal violet assays showed the most reproducible results with IC<sub>50</sub> values for CoCl<sub>2</sub> in the range of ~300 $\mu$ M. Interestingly, further experiments using BrdU incorporation to assess proliferation suggested that cardiac fibroblasts were more sensitive to CoCl<sub>2</sub> treatment than Swiss 3T3s. In the former, after either 48h or 72h there was ~80% reduction in proliferation with 25 $\mu$ M CoCl<sub>2</sub> and almost no proliferation following 100–150 $\mu$ M CoCl<sub>2</sub>. Cell viability in increasing concentrations of CoCl<sub>2</sub> (up to 500 $\mu$ M) was assessed using CFDA and propidium iodide staining. The ratio of live:dead cells decreased dramatically with increasing CoCl<sub>2</sub>. Phalloidin-FITC was also used to examine cell viability and structure following treatment. With increasing CoCl<sub>2</sub> there was evidence for increased disruption of actin filaments. In conclusion, short-term low dose CoCl<sub>2</sub> treatment of ventricular preparations results in compromised contractile function. Treatment of non-contractile cardiac fibroblasts with higher concentrations results in decreased ability of cells to proliferate as well as long-term cell damage and death. It is likely that the cardiotoxic effects of CoCl<sub>2</sub> are manifest in both contractile and non-contractile cells of the heart. The underlying cellular mechanisms involved have yet to be established.