

## Tobacco smoking-induced toxicity in cardiomyocytes derived from human pluripotent stem cells

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Cigarette smoking is an important risk factor for heart disease. Mechanistically-relevant biomarkers could provide timely assessment of the toxicity of tobacco products, including new products that wish to make claims with reduced health risks. The goal of this study is to investigate toxic effects and identify biomarkers of harm in induced pluripotent stem cell (iPSC)-derived human cardiomyocytes. Two cigarette smoke condensate (CSC) concentrations were tested: Low (10 µg/ml) and high (30 µg/ml) following 1-30 day exposures. RNA was isolated at defined time points (1, 7, 14, 30 days) and global gene expression was analyzed using next-generation sequencing. Exposure of cardiomyocytes to CSCs resulted in significant changes to multiple pathways. The Nrf2-mediated antioxidant stress pathway was consistently upregulated across all time points. Moreover,