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Fat mass and obesity-associated gene (FTO) hypermethylation induced by decabromodiphenyl ethane causing cardiac dysfunction via glucolipid metabolism disorder

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Background:
Decabromodiphenyl ethane (DBDPE), a type of bromine flame retardant (BFR), which is the major alternative to BDE-209 owing to its lower toxicity. In recent years, DBDPE has aroused people's concern owing to its ecological persistence and durability. Until date, DBDPE was reported to possess neurotoxicity, hepatotoxicity, and disturb thyroid functions. However, the effect and mechanism of DBDPE on cardiotoxicity have rarely been studied.

Objective: In the present study, we investigated the impacts of DBDPE on the cardiovascular system in male SD rats and then explored the underlying mechanisms to explain the cardiotoxicity of DBDPE using AC16 cells.

Methods: Under in vivo conditions, male rats were administered with an oral dosage of DBDPE at 0, 5, 50, and 500 mg/kg/day for 28 days, respectively.

Results:
DBDPE could thus decrease the level of MYH6 and increase the level of SERCA2. Furthermore, DBDPE could increase the serum levels of glucose and low-density lipoprotein but decrease the content of high-density lipoprotein. In addition, DBDPE could activate the PI3K/AKT/GLUT2 and PPARγ/RXRα signaling pathways in AC16 cells. In addition, DBDPE decreased the UCP2 level and ATP synthesis in mitochondria, consequently leading to apoptosis. Bisulfite sequencing PCR identified the hypermethylation status of FTO. Findings: These results suggested that FTO hypermethylation played a regulative role in the pathological process of DBDPE-induced glycolipid metabolism disorder, thereby contributing to the dysfunction of myocardial contraction and relaxation through cardiomyocytes fibrosis and apoptosis via the mitochondrial-mediated apoptotic pathway resulting from mitochondrial dysfunction.

Conclusion: The demethylation of FTO in the cardiomyocytes may thus offer a novel molecular target toward preventing DBDPE-induced cardiotoxicity and thereby providing a new treatment strategy to alleviate cardiac dysfunction induced by DBDPE.

Biography

Jialiu Wei has engaged in protection of reproductive and cardiovascular health. He specialized in environmental toxicology, preventive cardiology, and epidemiology as well. He conducted the research of signal transduction pathway of environmental organic pollutants-induced cardiovascular diseases development, and mechanism of reproductive injury induced by atmospheric fine particulate matter. He also modified behavioral factors on the health impact of environmental factors. Other research interests include adverse health effect of mixed organic pollutants, identification of significant exposure pathways and their impact on health, and pesticide residue relevant to human health.

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