Keynote Speech

Transgenerational epigenetic inheritance: focus on endocrine disrupting chemicals and male reproductive hazards

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Dr. Hsu has a Ph.D. degree in Basic Medical Sciences (1998) from National Cheng Kung University Medical College, Tainan, Taiwan. His research in occupational and environmental health is primarily focused on (1) male reproductive effects of endocrine disrupting chemicals (Pb, PCBs, DEHP, and PBDEs) in animals and epidemiological studies, (2) animal and human effects and biomarkers of $PM_{2.5}$/air pollutants, and (3) sperm DNA methylation and epigenetic transgenerational effects after prenatal exposed to DEHP and PBDEs in rats.

Bibliography:

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Abstract：

Endocrine disrupting chemicals (EDCs) exposures such as plasticizer, di(2-ethylhexyl) phthalate (DEHP), might promote the epigenetic transgenerational inheritance of male reproductive hazards. Progress in understanding epigenetic mechanisms opens new perspectives to estimate the risk of EDCs. In this study, we test the hypothesis to compare the effects of transgenerational epigenetic inheritance between maternal exposure to low or high doses of DEHP on sperm functions and DNA methylation in male offspring. Pregnant rats were treated with 20 µg, 200 µg, 5 mg or 500 mg of DEHP/kg/day through gavage from gestation day 0 to birth. The offspring body weight, anogenital distance (AGD), anogenital index (AGI), sperm count, motility, and DNA fragmentation index (DFI) were measured for all generations. Methyl-CpG binding domain sequencing and whole-genome bisulphite sequencing (WGBS) were performed to analyze sperm DNA methylation status in the F3. DEHP exposure at 20 µg/kg affected AGD, AGI and mean DFI in the F1; sperm morphology in the F2; and ROS, mean DFI, and Dnmt1 in the F3. DEHP exposure at 200 µg/kg affected AGI, MMP and mean DFI in the F1; mean DFI in the F2; and ROS and mean DFI in F3. DEHP exposure at 500 mg/kg affected AGD, AGI, sperm count, mean DFI, and %DFI in the F1; AGD, sperm count, and mean DFI in the F2; and AGD, AGI, mean DFI, and %DFI in the F3. DEHP exposure at 5 mg/kg affected AGD, AGI, sperm count, and %DFI in the F1; sperm count in the F2; and AGD and AGI in F3. Compared with the control group, 24, 27, 15, and 45 differentially hypermethylated genes were identified in the groups 20 µg/kg, 200 µg/kg, 5 mg/kg, and 500 mg/kg DEHP, respectively. Moreover, 11,18, 130, and 6 differentially hypomethylated genes were observed in the groups administered 20 µg/kg, 200 µg/kg, 5 mg/kg, and 500 mg/kg DEHP, respectively. The field of epigenetic toxicology is new and its application in public health or in the understanding of disease etiology is almost non-existent. Overall, these results demonstrated that prenatal exposure to DEHP caused transgenerational epigenetic effects, which may explain the observed phenotypic changes in the male reproductive system.

Key words: Di(2-ethylhexyl) phthalate (DEHP); Male reproduction; Transgenerational effects; Epigenetics; Sperm DNA methylation