GS03-5 **The imprinting of defects in sexual behavior by maternal exposure to dioxin and its mechanism**

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Many forms of reproductive toxicity caused by 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) occur in pups whose mother is exposed to the lower doses of this substance. However, the toxic mechanism underlying these defects remains to be clarified in spite of many researches conducted so far. Our previous studies have provided evidence that the administration of TCDD (1 μg/kg, orally) to pregnant Wistar rats at gestational days 15 (GD15) causes a reduction in gonadotropin biosynthesis in the fetal pituitary and this reduction leads to the attenuated expression of steroidogenic proteins in the fetal gonads. Such attenuation occurred during a short period from GD20 to postnatal day 0. The supplementation of equine chorionic gonadotropin into the fetuses exposed to TCDD at GD15 restored not only the reduced expression of gonadal steroidogenic proteins but also defects in sexual behavior. To further clarify the mechanism of TCDD effect on fetal gonadotropin biosynthesis, we investigated whether TCDD can directly affect the fetal pituitary to reduce gonadotropin synthesis, using cultured pituitary. When cultured fetal pituitary was treated with TCDD in the presence of gonadotropin-releasing hormone, TCDD interfered with the induced expression of gonadotropin β-subunit. This observation suggests that the mechanism of TCDD effect on gonadotropin biosynthesis involves its direct action on the fetal pituitary. We are now focusing on comprehensive change in gene expression in the pituitary and its regulator organ, hypothalamus, following maternal exposure to TCDD.