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Isoflavone Exposure during Different Periods of Life Differentially Modulates Estrogenic Response of the Mammary Gland and the Fat Tissue

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Abstract:

The incidence of breast cancer in eastern Asia is approximately 3-times lower than in western countries. There is evidence that the traditional East Asian diet which is rich Isoflavones (ISO) like genistein (GEN), daidzein (DAI), and glycitein (GLY) seems to play an important role and that ISO intake must be during certain windows of development to exert anti-cancerogenic action. In this study we investigate the effects of soy ISO exposure in different periods of life on the estrogen sensitivity of the mammary gland in four defined groups of a rat animal model. Group 1 received lifelong an ISO-free diet (IDD), Group 2 lifelong a ISO-rich diet (ISD). Group3 was exposed during puberty to an ISD from PND 30 up to PND 60; (pISD). In Group 4 adult animals were exposed to a diet enriched with an ISO extract (IRD 400) starting in the age of 80 days. In IDD, ISD and pISD onset of puberty, the menstrual cycle length andproliferative status of the mammary gland at day 50 were determined. The onset of puberty occurred significant earlier in pISD and ISD compared to IDD. Menstrual cycle length was significantly shortened in pISD. In intact animals at day 50 and day 80 the uterus wet weights were not affected by the respective diets. Proliferation in the mammary gland was not affected by IDD and ISD. To analyze the effect of ISO on the estrogen sensitivity of mammary gland, animals of all groups were ovariectomised at the age of 80 days. At the age of 94 days animals were treated for 3 days with estradiol. Interestingly proliferative response of the mammary gland towards E2 was significantly reduced in the pISD and ISD groups. In contrast a reduced response of progesterone receptor (PR) expression towards E2 could be only observed in the ISD group. In the IRD 400 group visceral fat tissue mass was significantly reduced by E2 treatment compared to the respective control group. In summary our results provide evidence that in female rats the exposure to ISO during puberty reduces the proliferative response to E2. In contrast regulation of PR expression by E2 is only affected following lifelong ISO exposure. Our preliminary data from fat tissue suggest that in addition other tissues than the mammary gland differentially responds to estrogens following dietary exposure to ISO. We hypothesize that the estrogen sensitivity of different endpoints relevant to critical periods of development are modulated by ISO. Investigation of the involved molecular mechanism is in progress.

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