Livelong isoflavone exposure dose dependently modulates the estrogen and androgen sensitivity of a variety of tissues in male and female wistar rats

Program: Abstracts - Orals, Featured Poster Presentations, and Posters
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The effects of isoflavones (ISO) on tumor risk, reproduction and the susceptibility to develop metabolic diseases are controversially discussed. To investigate whether lifelong exposure to ISOs modulates the hormone sensitivity of different tissues towards estrogens and androgens we initiated a dose-dependent animal study. Throughout their whole development, from embryo to adulthood, male and female Wistar rats were exposed to different diets enriched with varying concentrations of a special soy extract (Novasoy650®): ISO-depleted diet (IDD), IRDlow (55 ppm Dai+Gen, calculated as aglycone) and IRDhigh (460 ppm Dai+Gen, calculated as aglycones).

Hormone sensitivity of adult animals was tested in the design of either an uterotrophic assay or a Hershberger assay.

In female animals IRD dose-dependently induced earlier puberty onset. IRDhigh, but not IRDlow decreased estrus cycle length and prolonged the estrus phase. Treatment of ovariectomised (OVX) adult female rats with 17b-estradiol (E2) resulted in a significant increase of uterine wet weight, proliferative activity of the uterine epithelium and uterine and vaginal epithelial height. Responsiveness of theses endpoints to E2 was increased in IRDhigh animals compared to IDD and IRDlow animals.

In the mammary gland treatment of OVX animals with E2 stimulated proliferation (PCNA expression) and expression of the progesterone receptor (PR). Animals exposed lifelong to IRDhigh, but not IRDlow showed a decreased responsiveness. The visceral fat mass (VFM) in OVX as well as in E2 treated animals was lowest in the IRDhigh group.

In castrated (ORCHI) male animals treatment with testosterone propionate (TP) increased seminal vesicle, prostate and levator ani weight. Rats lifelong exposed to IRD showed an increased responsivness of the seminal vesicles, the levator ani and the tibia. TP treatment decreased VFM in ORCHI animals. Interestingly VFM of untreated IRDhigh animals was as low as observed in TP treated animals.

In summary our data provide evidence that lifelong ISO exposure dose-dependently modulates the sensitivity of a number of tissues in male and female rats towards sex steroids. This observation is relevant to understand the effects of lifelong ISO exposure on tumor risk, reproduction and the susceptibility to develop metabolic diseases.