Soy Isoflavones are positively associated with Human Tissue Levels of 17β-Estradiol in Mammoplasty Specimen but do not affect Fluxes of Estrogen-DNA Adducts determined by Computational-based Metabolic Network Modelling

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17β-estradiol contributes to breast cancer development by induction of proliferation and/or DNA adduct formation. Since beneficial and adverse effects of isoflavones are discussed extensively, their influence on estrogen levels and on fluxes of estrogen-DNA adducts was investigated in 47 mammoplasty specimen.

Fluxes of estrogen-DNA adducts were determined by computational-based metabolic network modeling, comprising of 142 reactions of estrogen metabolism and 66 reactions of energy metabolism, using levels of 17β-estradiol and estrone, determined by GC-MS/MS, and transcript levels, determined by TaqMan® qPCR (estrogen metabolism) and RNA sequencing (energy metabolism) as flux constraints.

Besides adduct fluxes, dependent variables investigated by stepwise forward selected multiple linear regression models were 17β-estradiol, estrone and 17β-hydroxysteroid dehydrogenase type 2 (oxidation of 17β-estradiol to estrone). Explanatory variables (ExVARs) tested were intake of estrogen-active drugs, smoking, body-mass-index, age, lobular regression, oil and adipocyte content as well as transcript levels (estrogens only). The isoflavones genistein and daidzein were quantified using UHPLC-MS/MS and sum of both was used to generate the ExVAR "aglycones".

"Aglycones" was significantly positively associated with 17β-estradiol and significantly negatively with estrone as well as (borderline significantly) with transcript levels of 17β-hydroxysteroid dehydrogenase type 2. Yet, metabolic flux to estrogen-DNA adducts was not affected by isoflavones.

Supported by DFG, Le-1329/10-1

Journal of International Society of Antioxidants in Nutrition & Health; Volume 3, Issue 4 (2016) 10th World Congress on Polyphenols Applications: Porto Polyphenols 2016 DOI: http://dx.doi.org/10.18143/JISANH_v3i4_1340