

EFFECTS OF PHYTOESTROGENS ON THE OVARIAN AND PITUITARY PHENOTYPES OF OESTROGEN DEFICIENT FEMALE AROMATASE KNOCKOUT MICE

K. L. Britt^{1,2}, E. R. Simpson¹, J. K. Findlay¹

¹Prince Henry's Institute of Medical Research, Clayton, VIC, Australia; ²Monash University, Department of Biochemistry and Molecular Biology, Clayton, VIC, Australia

Phytoestrogens can induce both estrogen agonistic and antagonistic effects, depending on the tissue, estrogen receptor content and endogenous levels of estrogen. Dietary phytoestrogens are promoted as alternatives to synthetic estrogens for hormone replacement therapy, however their effects on the reproductive axis have not been exhaustively studied in vivo. Female aromatase knockout mouse (ArKO) mice are estrogen-free, and anovulatory with a block in folliculogenesis, hemorrhagic cysts and development of Sertoli cells within their ovaries. We evaluated the ArKO mouse as a model to test the effects of phytoestrogen-supplemented diets on the reproductive organ weights, ovarian morphology, gonadotropin levels and the transcript levels of ovarian somatic cell and steroidogenic markers. The extent to which phytoestrogens either as soyfree or soymeal diet or genistein added to a soyfree diet, exert estrogenic effects varied with the type of phytoestrogen and the parameter being tested. The genistein diet significantly increased uterine and ovarian weights of ArKO compared to wildtype mice, whilst both the soy, and to a larger extent the genistein diet, improved ovarian morphology compared to the soyfree diet. Transformation to morphological Sertoli cells in ArKO mice was decreased by both phytoestrogen diets, whilst the gene expression of Sertoli cell markers was not affected. The soy diet increased both LH and FSH in both genotypes compared to animals on the soyfree diet. The genistein diet reduced FSH levels in ArKO mice, correlating with increased ovarian inhibin subunit expression. In conclusion, phytoestrogens are estrogenic in ArKO mice. Specifically, they can affect serum gonadotropin levels, and offset the development of Sertoli cells and hemorrhagic cysts within the ovaries, depending on the type of dietary phytoestrogen. Further studies are required to determine the effective doses and treatment regimes for phytoestrogens as endocrine modulators. *Supported by NH&MRC Reg Key#198705.*