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Oestrogen receptor genotype modulates response of P1NP, a marker of bone formation to dietary isoflavone intervention in European postmenopausal women

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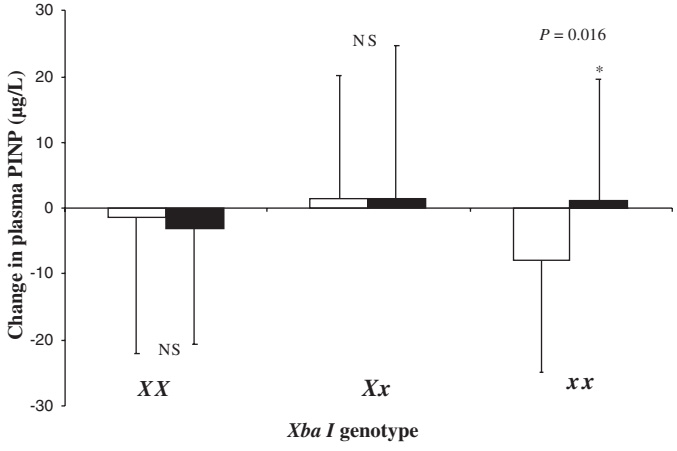
Isoflavones (IF) are soy-based dietary compounds that possess oestrogenic activity via interaction with the oestrogen receptors (OR). The evidence that IF may exert a protective effect against postmenopausal bone-loss from intervention studies is mixed; however, two recent meta-analysis suggest an overall significant effect of IF supplementation on increasing spinal bone mineral density (BMD) and decreasing bone turnover[1,2]. Polymorphisms in the OR gene may modulate the response of bone to IF supplementation. For example, Hall *et al.* showed a significant interaction between dietary IF and the OR beta (ORβ) gene in relation to cardiovascular health parameters[3].

Baseline data was obtained on nutrient intake, serum 25-hydroxyvitamin D, urinary (u) pyridinoline, u-deoxypyridinoline, plasma (p) bone-specific alkaline phosphatase and p-aminoterminal propeptide of type I collagen (P1NP), whole body and lumbar spine BMD from European postmenopausal women (*n* 242) who participated in a 12-month IF (110 mg/d) intervention study (PHYTOS). Polymorphisms in the OR alpha gene (ORα; *Xba*I and *Pvu*II) and ORβ gene (*Alu* II) were assessed using PCR and restriction digests. Multiple-regression analysis was used to test baseline associations between genotypes and bone indices, and possible genotype–IF treatment interactions on changes in bone parameters over the 12 months.

IF intervention had no significant effect on BMD and/or biochemical markers of bone turnover in postmenopausal women. There were no significant baseline associations between ORα and ORβ genotypes and BMD and/or bone markers. The two ORα genotypes, *Xba*I and *Pvu*II, modulated the effect of IF supplementation on plasma P1NP ($P = 0.002$ and $P = 0.030$, respectively) such that women with xx (*Xba*I) and pp (*Pvu*II) genotypes responded to IF treatment with significantly higher plasma concentrations of the bone-formation marker P1NP, compared the placebo group ($P = 0.016$ and $P = 0.003$, respectively; Table 1). There were no significant BMD or bone marker differences within the other *Xba*I or *Pvu*II genotype groups nor the ORβ genotype.

While IF intervention did not significantly affect bone health parameters in the overall cohort, stratification of subjects on the basis of ORα (*Xba*I, *Pvu*II) genotype showed a significant effect of IF supplementation on p-P1NP. It is unclear why p-P1NP was the only bone marker to respond to IF supplementation, and further investigation is required to increase our understanding of these complex genomic interactions and their implications on bone health.



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