

Letter to the Editor

## Possible permanent down regulation of oestrogen receptor expression during fetal life and breast cancer risk

Sir

Oestrogen production rates in blood levels are higher among white American than among Chinese women (Bernstein et al, 1990) and higher oestrogen levels have been associated with higher risk for breast cancer (Lipworth et al, 1996; Toniolo, 1997). Thus, the recent finding (Lipworth et al, 1999) that oestrogens during pregnancy are higher among Chinese than among white American women appears to contradict the hypothesis that pregnancy oestrogens are positively associated with breast cancer risk in the offspring, because the incidence of breast cancer is five times higher among American than among Chinese women. A possible explanation, however, for the apparent contradiction is down-regulation of oestrogen receptor expression during fetal life in response to higher circulating levels of oestrogens. If this were to be true, one should expect lower expression of oestrogen receptors among Chinese women than among American women in response to higher circulating oestrogen levels in the former group.

Two lines of evidence suggest that this may, indeed, be the case. Oestrogen receptor expression in breast cancer tumours is much lower among Asian than among Caucasian breast cancer patients (Nomura et al, 1984; Stemmermann, 1991). Moreover, in a study of normal women in the UK, oestrogen receptor expression in normal breast tissue was substantially higher among European than among non-European women (Ricketts et al, 1991). Since exposure to sex steroids during perinatal life has irreversible effects in experimental animals (Verhoeven et al, 1982), the explanation for the profound differences in breast cancer incidence between Western and Oriental women may be the permanent down-regulation of oestrogen receptor expression in fetal human breast tissues, under the influence of variable levels of pregnancy oestrogens.

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