Comment re: Premenopausal Mammographic Density and Hormone Levels

To the Editor: Mammographic density and ethnicity are two of a handful of factors very strongly associated with breast cancer risk, the others being major genetic influences and age (due to accumulation of somatic mutations). Genetic influences aside, levels of endocrine factors implicated in breast cancer etiology would be expected to be positively associated with mammographic density and be higher in population groups with substantially higher incidence of breast cancer, notably Caucasian women in North America in comparison with Chinese women in Asia. In their elegant investigation among premenopausal women, Walker and colleagues (1) found that high mammographic density is, as would be expected, positively associated with levels of estrogens and insulin-like growth factor I (IGF-I), but, unexpectedly, negatively associated with IGF-II levels. In a study comparing determinants of fetal growth in Caucasian and Asian women (2), cord blood IGF-I was significantly higher among Caucasian compared with Asian offspring, whereas the opposite was true with respect to IGF-II. Moreover, fetal growth was dominated by IGF-I in Caucasian offspring, but by IGF-II in Asian offspring. It has been documented that fetal growth, as reflected in birth weight, predicts breast cancer incidence several decades later (3). It appears that a shift in the balance of IGF-I and IGF-II in favor of the latter may be associated with lower risk for breast cancer, and the collective evidence from the relevant studies appears compatible with this proposition, at least with respect to premenopausal women (4, 5). In view of the findings by Walker and colleagues (1), the study of IGF-II (in conjunction with IGF-I and their binding proteins) in relation to breast cancer risk deserves more attention than it has received so far.

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Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References
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Cancer Res 2010;70:1743. Published OnlineFirst February 9, 2010.

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doi:10.1158/0008-5472.CAN-09-3311

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