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Letters

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Letters To The Editor: Comments on *Prebiopsy Neo-adjuvant Endocrine Therapy for Breast Cancer to Prevent Post-surgery Trauma-induced Growth Factor and Immune-suppression Mediated Tumour Progression,* Oliver *et al., Eur J Cancer,* 32A, No. 3, pp. 396–397, 1996

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I READ WITH interest the article by Oliver and colleagues in which the authors suggested the need for a new direction in breast cancer management in order to improve outcome [1]. Although I agree with the authors that neo-adjuvant endocrine therapy should be evaluated in prospective randomised trials, as this approach has a stronger biological rationale than neo-adjuvant chemotherapy, I feel that the authors' suggestion on the effect of immunosuppression following surgery and/or radiotherapy is rather superficial and lacks evidence. The authors' argument that immunosuppression enhances oncogenesis is probably applicable to all other major cancers, but not breast cancer.

There is a convincing body of evidence that, in women who develop breast cancer, there is an immune promotion of oncogenesis. At least eight studies have shown that the immunoreactivity in patients with an increased risk of developing breast cancer is higher than in healthy cohorts [2], and Robinson and associates found that natural killer (NK) cell activity was higher in women treated for bilateral breast cancer and decreased with adjuvant tamoxifen therapy [3]. The number of CD4 cells and the CD4/CD8 ratio also decreased with tamoxifen treatment. It is likely that depletion of these immunocytes promotes resistance to primary cancer growth and metastases. The prolonged lymphopenia following radiotherapy [4] may be one of the mechanisms by which radiotherapy exerts its effect in reducing breast cancer recurrence rather than being a reason for radiotherapy failure in prolonging survival, as Oliver and colleagues suggested in their article [1]. Although the individual radiotherapy trials failed to demonstrate a significant survival benefit in breast cancer patients, a meta-analysis of these trials perhaps reflects such a benefit.

Wei and associates reported a 30% reduction in breast cancer incidence in immunosuppressed mice [5]. Stewart and colleagues found a similar reduction (25%) in breast cancer incidence in women chronically immunosuppressed after organ transplantation (no change, $P < 0.009$) [6]. However, it remains unknown which part of the immune system may mediate this role. Growth factors and cytokines, such as interleukin-6 (IL-6), are particularly important in this context. Evidence has accumulated that breast tumours produce growth factors and cytokines, such as IL-6, insulin-like growth factor type 1 (IGF-I), IGF-II and tumour necrosis factor-alpha, which stimulate oestrogen synthesising enzymes in the breast tissue surrounding the primary cancer [7, 8], thus creating an oestrogenic environment that promotes breast carcinogenesis.

As lymphocytes and macrophages infiltrate within and around the tumour and the surgical wound following tumour excision, it is likely that these immunocytes may be the source of the growth factors and cytokines which promote locoregional recurrence, and future modulation of these factors may improve locoregional control. It can be concluded from the above discussion that immunosuppression in breast cancer may be more desirable than Oliver and colleagues have suggested.

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