LETTER TO THE EDITOR

Re: Modulation of basal and squamous cell carcinoma by endogenous estrogen in mouse models of skin cancer

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Dear Sir,

We thank Dr De Giorgi et al. for their letter and for the appreciation of our recently published work (1). We do believe that endogenous estrogen may have a protective role for melanoma also. We take the occasion, since there are no specific questions or concerns raised in the letter, to acknowledge the fact that our studies have been greatly facilitated by the use of powerful mouse models of non-melanoma skin cancer (2,3). Unfortunately, such resource is not yet available for malignant melanoma. We think that the results on the profound influence of hormones on epithelial skin cancer (i.e. basal cell carcinoma and squamous cell carcinoma) should strongly stimulate experimental studies of the factors influencing the far more deadly skin melanoma. Because the role of estrogens in melanocytic lesions is still unclear, development of genetically engineered mouse models that accurately recapitulate the essential features of the human disease should be a primary objective. These models would offer unique opportunities to investigate cancer mechanisms in genetically defined and environmentally controlled settings in the context of the tumor microenvironment and an intact immune system (4). These are critical distinctions from the widely used xenograft/transplant models in which several factors prevent faithful recapitulation of the human disease, e.g. additional mutations occurring in the selection of cell lines in vitro, site of injection in a different environment from the tumor in vivo, inappropriate developmental stage of the mice at the time of injection and their immunosuppressed condition. Obviously, accurate animal models would usefully complement, not replace, studies in humans.

On more general ground, we take the opportunity to comment on the fact that gender differences in skin cancer may be more widespread in nature than usually thought: a survey of the literature shows evidence that male sex is a risk factor for melanoma and non-melanoma skin cancer in fish. Epidermal papillomatosis developing as a consequence of environmental stress in the roach Rutilus rutilus is consistently higher in males than females (5,6), and intriguingly, a melanoma oncogene can be conserved in male swordtail fish because of its beneficial role in sexual selection, being linked to a pigment pattern that functions to increase mating success (7).

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References


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