Mononuclear Infiltrates in Osteosarcoma and Chemokine Receptor Expression

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To the Editor: Laverdiere et al. recently reported the expression of a series of chemokine receptors in osteosarcoma (1). The authors used real time PCR analysis to characterize the expression of chemokine receptors in osteosarcoma tumor tissue. The expression of CXCR4, CCR7 and CCR10 was correlated with overall patient survival, event free survival and metastasis free survival respectively. As stated in the manuscript, the authors were not able to verify receptor expression on the protein level (1).

We have recently performed immunohistochemistry analysis for chemokine receptors on a series of archival osteosarcoma samples. To corroborate the immunohistochemistry results, TaqMan RT-PCR analysis of mRNA expression levels was performed in parallel following micro dissection of the tumor samples. Importantly, our results show that infiltrating cells often represent a significant, or even the only source of chemokine receptor expression signal in osteosarcoma tissue. In contrast to Lavediere et al. we could demonstrate both CCR5 and CXCR3 expression on mRNA and protein level in osteosarcoma tumor samples. While CCR5 was shown to be expressed by both osteosarcoma cells and the mononuclear infiltrate, CXCR3 was only expressed by the infiltrating immune cells. Pronounced expression of CCR7 was demonstrated on an atypical mononuclear infiltrate. The receptor CCR1 was found on polynuclear giant cells as well as mononuclear infiltrating cells (Fig. 1).

These results demonstrate the danger of using mRNA analysis alone when determining chemokine receptor expression in tumor samples. Infiltrating mononuclear cells are an excellent source of virtually all chemokine receptors including CXCR4, CCR7 and CCR10 (2). Finally, the results suggest that the correlation of clinical outcome demonstrated using mRNA levels may be based al least in part, on the subtype and overall level of accompanying mononuclear infiltrate, clearly an important issue when using the receptors for the identification of prognostic or even therapeutic targets in tumor biology.

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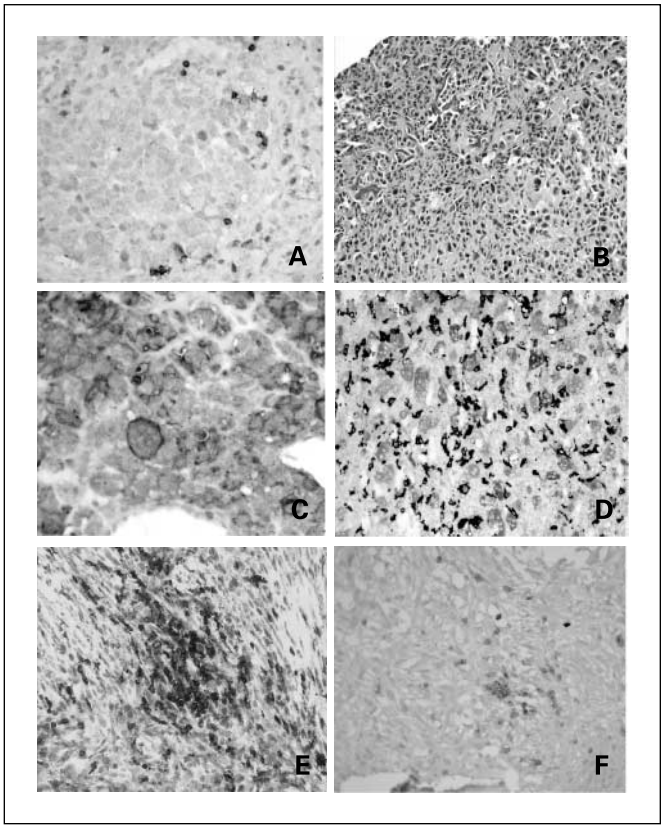

Fig. 1. Chemokine receptor staining in osteosarcoma. A series of osteosarcoma tumor samples were stained with monoclonal antibodies directed against CD3 (Becton Dickinson), CCR1, CCR7, CCR5 and CXCR3. Antigen was retrieved from archival fixed sections of osteosarcoma samples using established protocols for each antibody (3–5). *A,* scattered CD3-positive infiltrating cells were detected (×200). *B,* HE-staining of a pleomorphic osteosarcoma shows abundant osteoid production and highly pleomorphic, atypical mononuclear cells (×400). *C,* benign-looking giant cells found to express CCR1 as well as atypical mononuclear cells (×400). *D,* the expression of CCR7 in atypical mononuclear cells and some giant cells between some filigree and arborizing osteoid (×400). *E,* circumscript expression of CCR5 in a small follicular-like infiltrate (×400) as well as some tumour positivity. *F,* scattered expression of CXCR3 in infiltrating cells (×400) with negative stain of tumor.

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