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LETTER TO THE EDITOR

Cutaneous carcinosarcoma and the EMT: to transition, or not to transition? That is the question

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To the editor:

We thank Dr. Zidar and Dr. Gale for their timely and detailed comments on our paper [1]. Indeed, epithelial-mesenchymal transition (EMT) is a multifaceted process driven by an intricate network of molecular mechanisms which to date remain incompletely understood, due to the extraordinary complexity of their regulation [2]. These processes include changes in cell adhesion and shape, gene expression, and extensive cross-talk between signaling pathways that create complex biochemical networks [2, 3], of which the final result in cancer is the development of mesenchymal-like cells with enhanced capacity for invasion, migration, and dissemination [3].

Even though some authors have proposed that phenotypic modulation in tumor progression is a reflection of genomic instability rather than an EMT-driven process [4], we strongly believe that there is compelling evidence suggesting a key role of EMT in the biology of tumor progression. As we proposed in our paper, primary carcinosarcomas of the skin are rare biphenotypic cutaneous tumors which simultaneously express both epithelial and mesenchymal elements, suggesting that in their development an EMT process might be involved [5]. We explored this possibility by assessing loss of E-cadherin expression and upregulation of vimentin expression, a pattern that is considered to be the hallmark of EMT changes in epithelial cells [5]. However, we do agree that more stringent criteria should be applied when assessing EMT-suggestive histological patterns.

As Zidar and Gale state, among the multiple criteria that should be assessed, the presence of spindle cell morphology is a sine qua non. Although different epithelial morphotypes of cutaneous carcinosarcoma exist (squamous cell or basal cell derived), the presence of a spindle cell component is obligatory and a feature of all cases we studied. In all cases we studied, β-catenin and E-cadherin were expressed in the cytoplasmic membrane of benign epithelium, while tumor cells showed decreased E-cadherin membranous expression along

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