

## Are Surgical Margins Significant in Assessing the Prognostic Markers for Lymph Node Metastases?

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I was pleased to read this interesting paper on “Expression of CD133 Correlates with Tumor Stage, Lymph Node Metastasis and Recurrence in Oral Squamous Cell Carcinoma” by Bonetti et al. [1]. However it would be exemplary if the authors could shed some light on the some of the queries raised below.

The estimation of CD133 expression on the “surgical margins” of the tumor could have given more accurate correlation between its expression in the tumor and lymph node metastases. This is because the authors clearly mention that human CD133 is a cell surface glycoprotein originally identified as a target of the AC133 monoclonal antibody developed for its ability to react with normal cd34+ hematopoietic stem cells. In head and neck tumors, the vast majority of these stem cells are found within a 100 µm- radius of a blood vessel. These stem cells depend on interactions with several components for their survival and these endothelial cells secrete factors that promote the self-renewal and survival of head and neck cancer stem cells [2,3].

The next question arises “Where is the blood vessels increased in solid tumors?” Growth of the solid tumors involves vascularisation and earliest stages of formation are controlled by diffusion of nutrients from and to the neighbouring tissues. Eventually, the concentration of these most essential nutrients fall below the critical level where cells find it difficult to sustain and a necrotic core develops in the centre of the tumor resulting in transient collapse of blood vessels. Following this, the growth rate of the tumor reduces due to lack of nourishment. This mechanism of nutritional supply has been studied extensively using various mathematical models [4,5]. As the tumor reaches its diffusion limited size it induces the neighbouring blood vessels in the tumor margins to grow towards it which helps it establish a network with the circulatory system which forms the basis and starting point of metastases. Following this there is uncontrolled and explosive growth of the tumour contributing to its inherent aggressive nature [5,6].

Recent studies even in cancers involving the other sites of the body state that angiogenesis rely on endothelium proliferation and

this endothelium cell proliferation is shown to be predominant at the periphery of the tumor.<sup>5</sup> Moreover previous cancer models also supported the fact that large preneoplastic areas do exist beyond the surgical margins and they result in causation of local recurrence and secondary cancers or metastases [2,3].

The authors attempt in investigating the significance of prognostic markers to clinical outcome is truly commendable. However assessing the surgical margins would have provided the true measure of the CD 133 levels especially with regards to lymph node metastases and would have reflected better on the clinical outcome of the patients.

### Ethical Approval

None.

### Conflict of interest

No conflict of interest to declare.

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