



## Letter to the editor

## Together consideration of microenvironment and tumor cells: Analysis of papers published in Oral Oncology



Involvement of microenvironment in cancer initiation and progression is a well-known event. Not only cellular but also non-cellular factors present in the microenvironment are responsible for the modulation of all the classical hallmarks of carcinogenesis [1]. In accordance to it, recent foundation of cancer biology believes in the 'Tissue organization field theory' rather than 'Somatic mutation theory' [2]. The meaningful progress in the field of cancer biology demands the investigations not only on cancer cells but also on the surrounding microenvironment. Independent research on microenvironment or cancer cell will not lead us to anywhere unless we investigate both the aspects together (same patient and sample). This aspect is of paramount importance in today's world as it will help in solving the extremely complex jigsaw puzzle of carcinogenesis. We believe that the world wide published research articles that considered both the aspects together are very less as compared to research done on individual aspects. Probably this could be one of the reasons why we are still not able to find single biomarker that can efficiently predict the malignant potential of oral potentially malignant disorders [3].

With this element in mind, we decided to investigate the current scenario of research articles published in Oral Oncology on oral cancer and precancer. One of the major focuses of the journal is basic science and translational research in the field of cancer biology. Based on the bibliometric analysis, Oral Oncology is currently the top most journals in the field of oral cancer. Hence, it is selected for the analysis. Articles published from the issue of January 2018 to June 2019 were retrieved and analyzed for together consideration on tumor cell and microenvironment. The abstracts as well as full text were thoroughly investigated by NC and GS, and disagreement on any paper was clarified in consultation with SS and SP.

Total 456 papers were published out of which majority were original research [291 (63.82%)] followed by letter to the editor [94 (20.61%)], review articles [55 (12.06%)] and others [corrigendum/erratum 6 (1.32%), editorials 4 (0.88%), perspectives 3 (0.66%), retraction notices 2 (0.44%) and commentary 1 (0.22%)]. Out of total 291 original research, 117 (40.21%) were related to treatment and 44 (15.12%) were on cancer biology. Only 3 (1.03%) of the articles have considered tumor cells and microenvironment together for studying cancer biology [4–6]. Out of total 55 review articles, 5 (9.09%) were related to treatment and 7 (12.73%) were on cancer biology while none of the articles considered tumor cells and microenvironment together.

In recent, the role of cellular microenvironment that include stromal cells are suggested as key contributing factors in plasticity and drug resistance in oral cancer and also other types of cancer. The link between stromal cells and cancer cells in the tumor microenvironment is depicted at various axis, including molecular, genetic, and epigenetic exchanges of information that ultimately shape up the pro-tumor microenvironment. Besides stromal cells, the existence of tumor initiating stem cells is predicted in the tumor microenvironment that may employ

molecular ligands exchange to help cancer cells to survive environmental pressures including drug resistance [7]. Finally, the role of the heterogeneous oral microbiome in the local niche of tumor that may also indirectly shape up the pro-tumor or anti-tumor microenvironment [1]. Therefore, future investigations at preclinical and clinical levels will be potential avenues to disrupt molecular pathways that essentially lead to dismantling the cellular linkages among stromal cells, tumor initiating stem cells, cancer cells within the tumor microenvironment. By adopting these comprehensive approaches, preclinical and clinical investigations will potentially witness in the successful development of new classes of drugs/inhibitors such as ligand mimetic, peptide mimetic, RNA mimetic, metabolite mimetic, exosome disrupters, monoclonal antibodies targeted to ligands shared by both stromal and cancer cells, pharmacological inhibitors of pro-tumor extra-cellular enzymes/proteins.

Present analysis realizes the dire need for the together investigations on the microenvironment and tumor cell together thus representing the tissue organization theory of carcinogenesis. Such efforts might have drastic change in our understanding of cancer biology of oral cancer and thus helps in our quest for finding suitable therapeutic targets.

### Funding source

None declared.

### Declaration of Competing Interest

None declared.

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<https://doi.org/10.1016/j.oraloncology.2019.06.005>

Received 4 June 2019; Accepted 5 June 2019

Available online 07 June 2019

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