Reply to "Regarding: Apoptosis Signaling Molecules as Treatment Targets in Head and Neck Squamous Carcinoma"

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We appreciate the comments by Meng-Lei Zhou, MS, and Guan-Jiang Huang, MD, and provide this response.

First, Zhou and Huang suggested that we could not conclude that head and neck squamous cell cancer (HNSCC) cells rely on inhibition of apoptosis for survival because we did not examine the association between BCL-family expression and patient survival. Though we appreciate the analyses performed by Zhou and Huang, we emphasize that our study did not propose that we use apoptosis molecules as biomarkers in the clinical setting. We examined whether the BCL-family signaling molecules remained intact and functional, and were thus potentially available in HNSCC cells as treatment targets for therapeutic agents that specifically act on these molecules. Two of our published works, including our recent article in Laryngoscope, support this[1,2]. We showed that the apoptosis effectors BAX and BAK1

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were expressed, and that we could induce apoptosis by using the inhibitors ABT-263 (navitoclax) and A1210477.

Zhou and Huang also suggested that we validate our findings in human tissues or animal experiments. We examined BCL2-L1, MCL-1, BCL-2, BAX, and BAK1 expression in both The Cancer Genome Atlas (TCGA), and gene expression data acquired at our own institution. We endorse that examining these datasets are sufficiently representative of RNA expression of these molecules in patient-derived HNSCC tumors. We agree that validation of protein expression of certain apoptosis signaling molecules, perhaps via immunohistochemistry, would be of interest. Specifically, papers we cited by Michaud, et al. [3] and Nichols, et al.[4] had previously focused on immunohistochemical expression of BCL-2 and BCL-xL in HNSCC. In regard to validation of our work in animal models, we fully agree with examining drug combinations that target apoptosis machinery for the treatment of HNSCC, and these animal studies are planned.

Zhou and Huang also suggested that our HNSCC cell line panel was limited because we did not include cells derived from larynx and thyroid cancer. We agree that including laryngeal squamous cancer cell lines would be of interest. Laryngeal cancers were included in our analysis of TCGA and our own gene expression dataset. As for thyroid cancer cell lines, on this point we respectfully disagree. Previous comprehensive studies have shown that the genomic and molecular background in thyroid cancers[5] are markedly different than HNSCC[6]. While it may be important to evaluate apoptosis signaling molecules as potential drug targets in thyroid cancer, this should be considered independently from studies focused on HNSCC.

References

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