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ABSTRACT

Adenoid cystic carcinoma (AdCC) comprises approximately 10% of all epithelial salivary gland neoplasms. AdCC is one of the most common salivary gland malignancies and the long-term prognosis is poor. In this study, we examined alterations of AdCC-associated genes, AdCC-associated genes, *MYB, MYBL1, MYBL2*, and *NFIB*, and their target molecules including MYC. The results were correlated to clinicopathological profile of the patients. Using paraffin tumor sections from 33 cases of salivary gland AdCC, we performed a detailed fluorescence *in situ* hybridization (FISH) analysis for gene splits and fusions of *MYB, MYBL1, MYBL2*, and *NFIB*. We found that 29/33 (88%) AdCC cases showed gene splits in either *MYB, MYBL1*, or *NFIB*. None of the cases showed an *MYBL2* gene alteration. AdCCs were genetically divided into six gene groups, *MYB-NFIB* (n=16), *MYB-X* (n=4), *MYBL1-NFIB* (n=2), *MYBL1-X* (n=1), *NFIB-X* (n=6), and gene-split-negative (n=4). AdCC patients showing the *MYB* or *MYBL1* gene splits were associated with microscopically positive surgical margins (p=0.0148) and overexpression of MYC (p=0.0164). MYC expression was detected in both ductal and myoepithelial tumor cells, and MYC overexpression was associated with shorter disease-free survival of the patients (p=0.0268). The present study suggests that 1) nearly 90% of AdCCs may have gene alterations of either *MYB, MYBL1,* or *NFIB,* suggesting diagnostic utility of the FISH assay, 2) *MYB* or *MYBL1* gene splits may be associated with local aggressiveness of the tumors and overexpression of MYC, which is one of the oncogenic *MYB/MYBL1* targets, and 3) MYC overexpression may be a risk factor for disease-free survival in AdCC.