Oral Abstracts Accepted for the 2020 American Academy of Oral Medicine Annual Meeting

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Lester Burket Memorial Award Presentations

Each year, residents of accredited US and Canadian oral medicine training programs compete to receive the Lester Burket Memorial Award for exemplary research. There are 2 award recipients this year:

THE INTERPLAY OF HYPOXIA AND AUTOPHAGY IN EPITHELIUM-DERIVED AMELOBLASTOMA CELL SURVIVAL: A PILOT STUDY

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Objectives: Ameloblastoma is the most clinically significant benign odontogenic tumor of the jaws. Ameloblastomas have a locally aggressive growth pattern and a high rate of malignant transformation. The etiopathogenesis of ameloblastoma is still unknown, and there is still a paucity of information on the factors regulating the locally aggressive growth characteristics of ameloblastoma. Hypoxia and autophagy are 2 mechanistic processes associated with tumor behavior as several tumor cells induce a hypoxic microenvironment to survive. Epithelium-derived ameloblastoma cells (EPAMCs) demonstrate enhanced basal autophagy, but the roles of hypoxia and autophagy in EPAMC survival and ameloblastoma recurrence are still unknown. To understand ameloblastoma pathogenicity and behavior, the goals of this study were to assess differential expression of ameloblastoma-specific and autophagy markers in primary and recurrent ameloblastoma and to assess the roles of hypoxia and autophagy in EPAMC survival. Our hypotheses were that ameloblastoma expresses markers similar to odontogenic epithelial tissue and hypoxia induces oxidative stress and activates autophagy in EPAMCs, favoring their survival and recurrence.

Methods: Primary and recurrent ameloblastoma tissues from 2 patients were immunostained with pan-cytokeratin, vimentin, and SQSTM1/p62 to assess the expression levels of ameloblastoma and autophagic markers. Additionally, EPAMCs were subjected to severe hypoxia (0.1% O_2) and then allowed to recover for 24 hours in order to define responsiveness to hypoxia based on expression levels of hypoxic (hypoxia-inducible factor [HIF]-1α), survival (phosphorylated extracellular signal-regulated kinase 1/2), and autophagic (Beclin1, phosphorylated 40S ribosomal protein S6 [pS6], SQSTM1/p62, LC3A/B) markers as detected by Western blotting. Previously characterized human odontoma-derived cells (HODCs) served as control odontogenic cells. All experiments were performed in at least triplicates. Data were analyzed as fold change relative to normoxia and expressed as mean $\pm$ standard deviation. A paired t test comparison of means was done to compare the expression of autophagy proteins when cells were under normoxia to protein expression under hypoxia and recovery conditions. The Welch 2-sample t test was used to compare fold changes from normoxia in EPAMCs and HODCs with each other. P values were adjusted for multiple comparisons using the Benjamini-Hochberg procedure.

Results: Both primary and recurrent tissue samples stained positive for pan-cytokeratin in the cytoplasm of the ameloblastoma islands. Vimentin and SQSTM1/p62 were undetectable in all samples, but the connective tissue stained positive for vimentin. Relative to normoxia, HIF-1α and SQSTM1/p62 expression was increased when the EPAMCs were reoxygenated ($P = .056$). pS6 levels were decreased in EPAMCs in both hypoxia ($P = .005$) and recovery ($P = .005$) compared with basal levels. Hypoxia, however, did not induce any significant changes among the remainder of the hypoxic, survival, and autophagic markers; no statistically significant difference was observed between the EPAMCs and HODCs.

Conclusions: The results of this pilot study provide insight into the pathogenicity of ameloblastoma and the possible behavior of EPAMCs when subjected to hypoxia. Our observation of vimentin expression alongside the pan-cytokeratin pattern is consistent with an epithelial origin of both primary and recurrent ameloblastoma. In EPAMCs, canonical autophagy tended to increase with hypoxia and did not recover when cells were reoxygenated, as evident by the increased HIF-1α and SQSTM1/p62 and the reduced levels of pS6 24 hours following hypoxia. This supports EPAMCs re-establishing basal autophagy after severe hypoxia and that recurrence of ameloblastoma may be related to autophagy.

REGULATION OF STAT4 BY ETS1 IN SJÖGREN SYNDROME PATHOGENESIS

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Objectives: Primary Sjögren syndrome (pSS) is a chronic autoimmune disease mainly affecting women over the age of 40, causing dry mouth and eyes. The etiology of pSS is complex and includes the overexpression of inflammatory cytokines from affected salivary gland epithelial cells (SGECs). Our group has previously identified candidate biomarkers overexpressed in salivary gland tissues of patients with pSS. We showed that ETS proto-oncogene 1 (ETS1) had higher mRNA and protein expression in pSS salivary glands that correlated with higher levels of lymphocytic infiltration. It has also been shown that the signal transducer and activator of transcription 4 (STAT4) gene contains pSS susceptibility polymorphisms and is