P10-4

A pH-sensitive Smart Material for Oral Squamous Cell Carcinoma Inhibition

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Background

Oral cancer is the eighth most prevalent cancer worldwide, and more than 90% of oral cancers are oral squamous cell carcinoma (OSCC). Dysregulated pH is emerging as a hallmark of cancer with an increased intracellular pH (pHi) and a decreased extracellular pH (pHe). In normal cells, pHe is about 7.4. However, the mean value for pHe is between 6.56 and 6.97 in oral cancer, suggesting an acidic microenvironment.

Materials and Methods

Here, we synthesized a pH-sensitive smart monomer named dodecylmethylaminoethyl methacrylate (DMAEM), which can consume H^+ in acid microenvironment, and studied the effect of DMAEM on proliferation, apoptosis, migration, invasion, and autophagy of Cal-27 cells (an OSCC cell line) in neutral (pH 7.3) and acidic (pH 6.7) culture medium.

Results

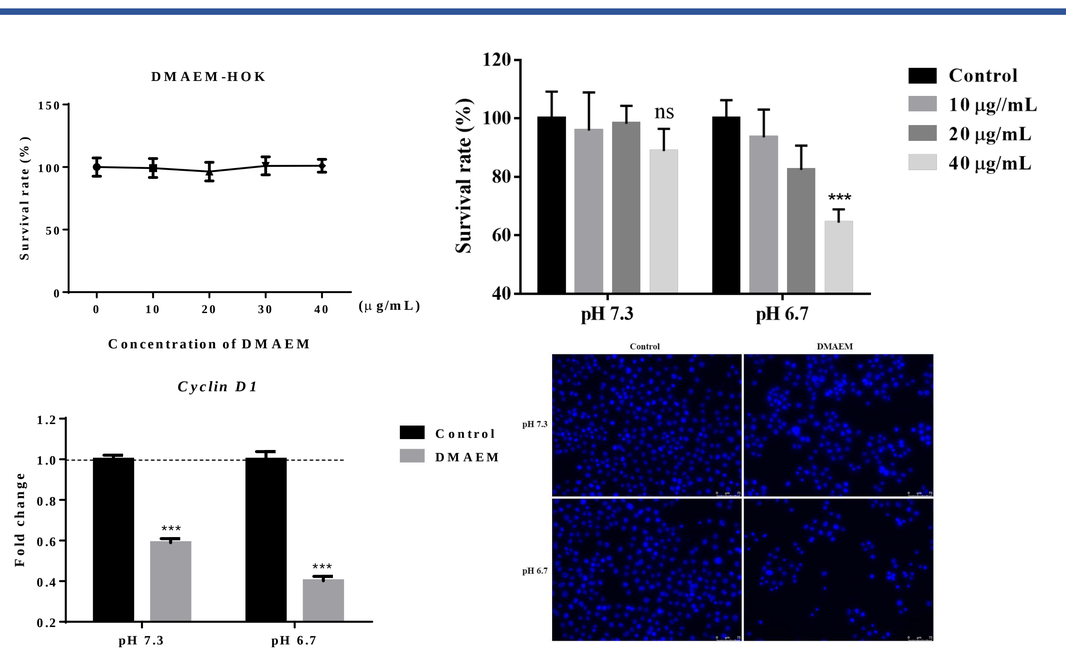


Figure 1. Effect of DMAEM on proliferation of Cal-27 cells. 40 μg/mL DMAEM had no toxicity on human oral keratinocytes, but inhibited proliferation of Cal-27 cells and down-regulated the expression of *Cyclin D1* in a pH-dependent manner.

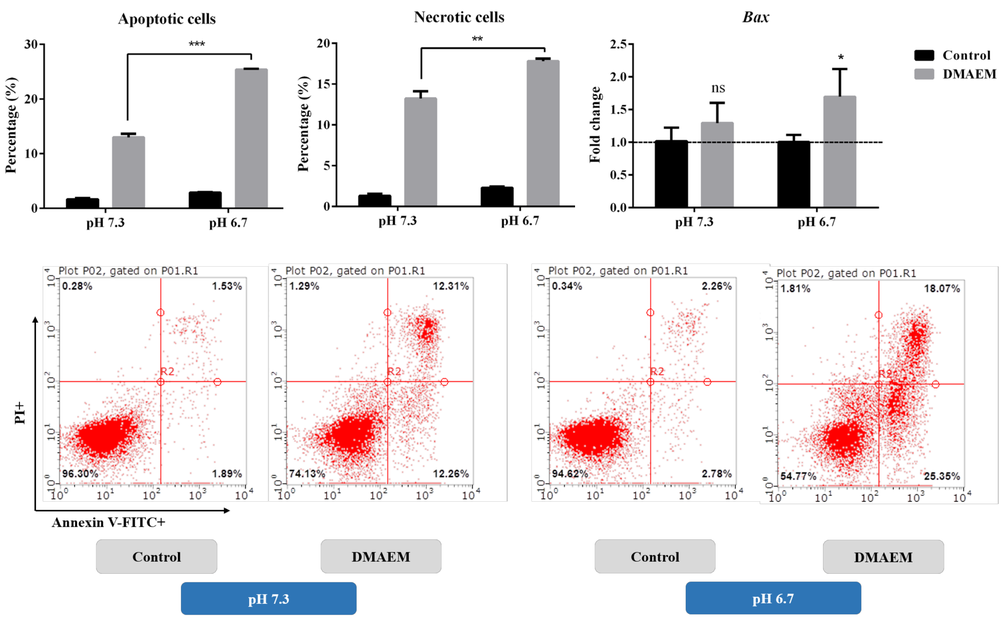
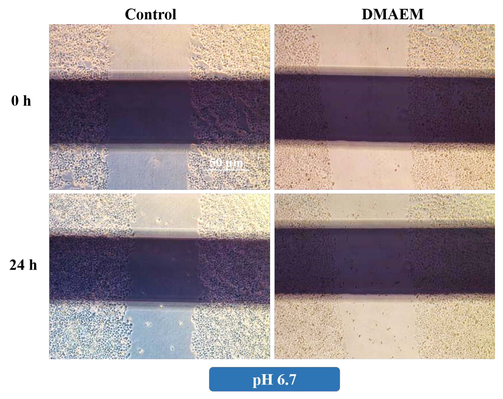


Figure 2. Effect of DMAEM on apoptosis of Cal-27 cells. DMAEM promoted apoptosis and necrosis of Cal-27 cells in a pH-dependent manner. Besides, gene expression level of apoptosis-related protein Bax was upregulated with DMAEM treatment.



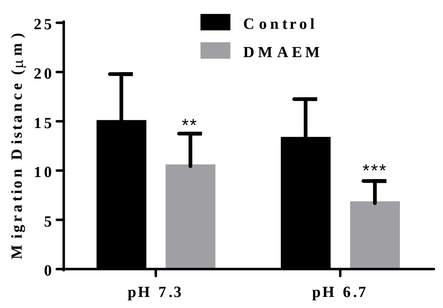


Figure 3. Effect of DMAEM on migration of Cal-27 cells. DMAEM inhibited migration of Cal-27 cells. In acidic environment, migration distance was shorter with DMAEM treatment compared to that in neutral environment.

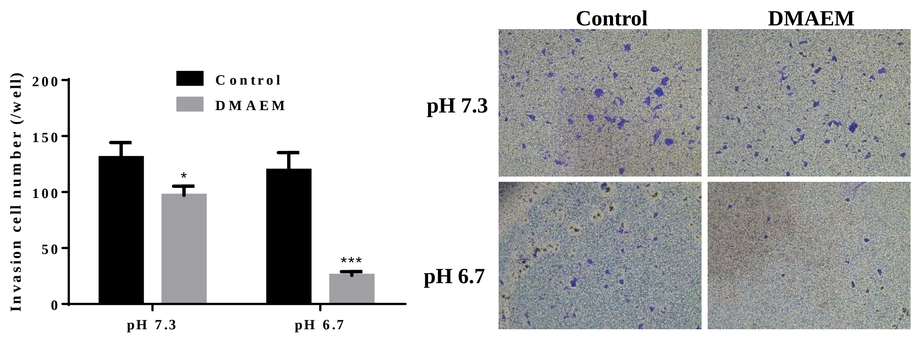


Figure 4. Effect of DMAEM on invasion of Cal-27 cells. DMAEM inhibited invasion of Cal-27 cells in a pH-dependent manner.

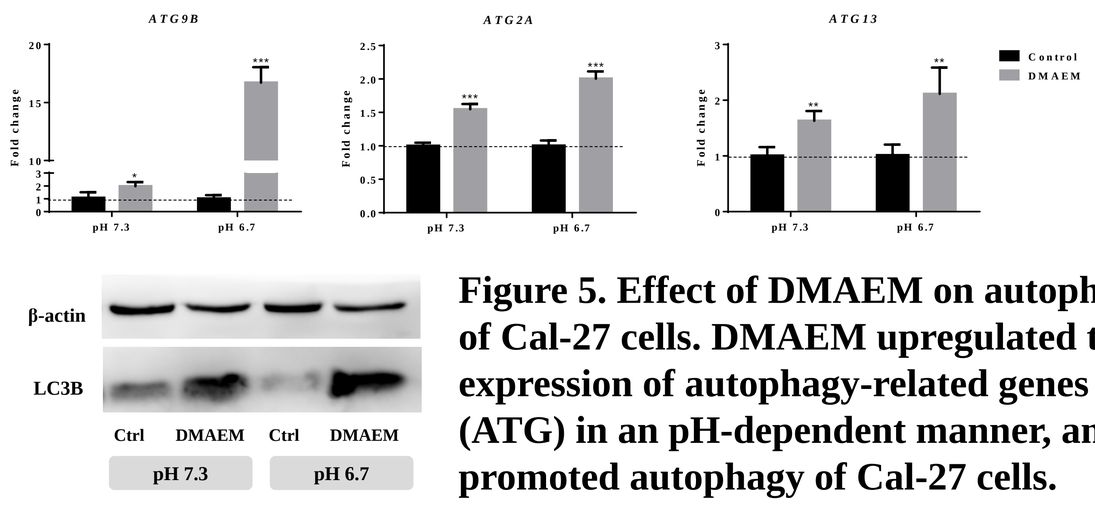


Figure 5. Effect of DMAEM on autophagy of Cal-27 cells. DMAEM upregulated the expression of autophagy-related genes (ATG) in an pH-dependent manner, and promoted autophagy of Cal-27 cells.

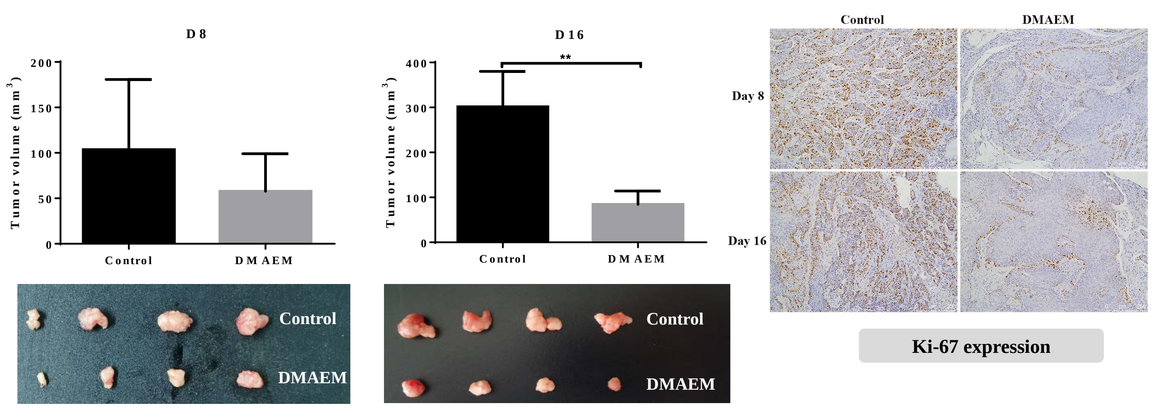


Figure 6. Effect of DMAEM on growth of OSCC in *vivo*. DMAEM inhibited growth of OCSS and down-regulated the expression of nuclear proliferation antigen Ki-67.

Conclusion

DMAEM inhibited proliferation, migration and invasion of Cal-27 cells, and promoted apoptosis as well as autophagy of Cal-27 cells in a pH-dependent manner. Besides, DMAEM inhibited the growth of Cal-27 tumors in *vivo*. In summary, our study focused on the acidic tumor microenvironment, and our data suggested the potential of DMAEM as a novel pH-sensitive smart material for oral cancer treatment.