TITLE: Functional characterization of CRTC1-MAML2 fusion oncogene

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RESEARCH PROJECT DESCRIPTION

Mucoepidermoid carcinoma (MEC) is the most common salivary gland malignancy and also arises in multiple other organ sites. Currently, patients with advanced, unresectable MEC have limited therapeutic options and poor treatment outcomes. We were the first to clone a novel fusion oncogene, CRTC1-MAML2 from a recurrent t(11;19)(q14-21;p12-13) in malignant MEC cells. The CRTC1-MAML2 fusion oncogene is associated with more than 50% of human MEC cases and represents a potential major etiologic molecular defect for MEC. We have shown that the CRTC1-MAML2 fusion protein has strong transcriptional co-activator activity and is capable of transforming epithelial cells in vitro, in part through co-activating the transcription factor CREB. Moreover, depletion of CRTC1-MAML2 fusion expression reduced the growth and survival of human malignant MEC cells when assayed in vitro or when propagated as xenograft tumors in vivo. These findings indicate that CRTC1-MAML2 is essential in maintaining MEC malignant phenotype and thus serves as a promising therapeutic target. However, the critical mediators and the in vivo roles of this fusion oncogene in the development and progression of MEC remain poorly elucidated. The goal of our project is to elucidate the role and mechanisms of CRTC1-MAML2 and explore approaches to block downstream oncogenic signals. This project is currently funded by the National Institute Of Dental & Craniofacial Research.

Medical student will participate in functional characterization of the downstream CRTC1-MAML2 target genes or testing of therapeutic agents, using various approaches such as cell culture, expression analysis, mouse models, and bioinformatic tools. In addition, we have other projects studying molecular basis of lung cancer and leukemia.

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