0302 Phenotype Characterization and Microarray Gene Expression Profile of Odontogenic Tumors

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Despite tremendous advances in our understanding of the molecular determinants governing normal tissue development, our knowledge of early events leading to tumorigenesis remains limited. The TgAC transgenic mouse over-expresses the V-Ha-ras oncogene driven by a zeta-globin promoter and readily develops odontogenic tumors. Objective: We hypothesize that the heterogeneous odontogenic tumor phenotypes observed in the TgAC mouse result from the differential expression of multiple genes. Methods: Tumors were harvested from 38 TgAC mice and evaluated histologically using light microscopy. Gene expression profiles were determined either by RT-PCR or using 16,000 gene custom printed cDNA arrays. Normal 4 day molar mouse tooth bud RNA was used as a reference tissue. Results: The tumors varied phenotypically from poorly differentiated tumors (Type 1), to plexiform ameloblastoma-like tumors with epithelial strands of cells (Type 2), to complex odontomas with mineralized dental tissues (Type 3). SAM analysis of the microarray data on four Type 2 tumors revealed 29 genes were significantly over expressed compared to tooth bud RNA. The tumors over expressed numerous genes associated with tumorigenesis (e.g. Dlk1, PEI98, Ctgf, Cdo1). The tumors showed multifold under expression of the tooth ECM proteins (AmelX, Enam, Dspp, MMP20, Klk4). Comparison of the poorly differentiated Type 1 tumor to the odontoma-like Type 3 tumor showed markedly different gene expression profiles. The Type 3 tumor showed much higher expression of the tooth ECM proteins while the Type 1 tumor over expressed numerous neuregic genes. Conclusion: Diverse odontogenic tumor phenotypes are associated with unique gene expression profiles that are likely responsible for establishing and maintaining tumor phenotype. Supported in part by NIDCR Grant # DE12879

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