**EXPLORING THE ROLE OF LONG NON-CODING RNA IN ORAL SQUAMOUS CELL CARCINOMA DEVELOPMENT AND THERAPY**

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**Abstract:**

**Background:** Oral Squamous Cell Carcinoma (OSCC) is the most common type of cancer in the head and neck region, yet current diagnostic and treatment strategies often prove inadequate. Despite advancements in treatment options, the overall survival rate remains approximately 50%, with even poorer outcomes in metastatic cases. As the quest for new biomarkers intensifies, long noncoding RNAs (lncRNAs) have emerged as significant players in cancer research. Recent studies indicate that lncRNAs are often abnormally expressed in various malignancies and are crucial for tumor growth and survival, making them promising candidates for cancer diagnosis and therapy. However, only a limited number of lncRNAs have progressed to clinical trials, and none have demonstrated effective outcomes thus far. The role of lncRNAs in OSCC remains underexplored, highlighting the necessity for comprehensive investigations into their functional and therapeutic significance.

**Materials & Methods:** To investigate the role of lncRNAs in OSCC, RNA sequencing analysis was conducted using patient samples, followed by validation through qRT-PCR. The candidate lncRNA gene was either overexpressed or knocked down in OSCC cell lines, and target molecules and pathways were identified using qRT-PCR, Western blot analysis, RNA pull-down assays, immunoprecipitation experiments, immunofluorescence microscopy, and luciferase assays. The therapeutic potential was assessed in OSCC mouse xenograft models following siRNA treatment. Data analysis and validation were performed using in silico methods and statistical analysis.

**Results:** The RNA sequencing analysis revealed a significant upregulation of 1,543 lncRNA genes and a downregulation of 986 genes in OSCC patient samples compared to adjacent non-tumor tissues. Additionally, gene ontology and pathway analyses identified several significantly altered categories, including "metabolic process," "PI3K-AKT pathway," "MAPK pathway," and "cell cycle pathway" in OSCC. Notably, we discovered a novel lncRNA, EGFR long non-coding downstream RNA (ELDR), which is significantly upregulated in OSCC samples. ELDR promotes OSCC cell proliferation by enhancing the expression of EGFR and Cyclin E1. When ELDR is overexpressed in normal oral keratinocytes (NOK), these cells gain a selective growth advantage for neoplastic transformation by fine-tuning FOXM1/AURKA signaling. Furthermore, intra-tumoral delivery of ELDR siRNA resulted in a regression of OSCC growth in mouse models.

**Conclusion:** The lncRNA ELDR may serve as a divergent gene in OSCC, and targeting this gene holds potential therapeutic significance.

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