Exploration of *ARID2* Gene Mutations in Oral Squamous Cell Carcinoma (OSCC): A Study of the Sri Lankan Cohort

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Oral squamous cell carcinoma (OSCC) is the most common type of oral malignancy in the world and represents a significant public health burden in South Asian countries, including Sri Lanka, where oral cancers show a significant percentage of all reported cancer cases. Despite advances in diagnosis and treatment, the molecular mechanisms underlying OSCC progression remain incompletely understood. Mutations in different cancer-associated genes are the main risk factors for tumorigenesis. *ARID2* (AT-rich interaction domain 2) is a gene that encodes a chromatin remodeling complex subunit and is considered a tumor suppressor gene. A novel finding in OSCC is the mutation of the *ARID2* gene, particularly in gingiva-buccal OSCC (GB-OSCC). However, the studies related to *ARID2* mutations in OSCC are limited and have not been conducted in Sri Lanka. Therefore, this study identified and characterized the specific *ARID2* gene mutations in OSCC samples collected within the Sri Lankan cohort. A total of 50 histopathologically confirmed oral biopsy samples were collected at the Dental Teaching Hospital, Peradeniya, comprising 15 OSCC, 30 potentially malignant disorders, and 5 healthy control samples. Genomic DNA was extracted, and the *ARID2* gene was PCR-amplified using intronic primers spanning exons 19 and 20. Amplified products were sequenced using Sanger sequencing, and the resulting sequences were aligned and analyzed in MEGA version 11 to detect mutations. Multiple sequence alignment identified a single point mutation in 1 of 15 OSCC samples (6.67%), located at chromosomal position chr12:169153, while no mutations were detected in the OPMD or healthy control groups. Fisher's exact test showed no statistically significant difference in mutation frequency between the three groups ($p = 0.398$), which likely reflects the low overall mutation frequency and limited sample size in this cohort. Nonetheless, this finding provides the first molecular evidence of an *ARID2* mutation within a Sri Lankan cohort. This mutation may potentially disrupt normal SWI/SNF chromatin remodeling complex function, which could contribute to dysregulated gene expression relevant to oral tumorigenesis. Overall, these findings establish a foundation for further investigation of *ARID2* as a molecular marker in OSCC and for exploring new avenues in OSCC research.

Keywords: *ARID2* Gene, chromatin remodeling complex, mutations, oral squamous cell carcinoma, tumor suppressor gene

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