

## ABSTRACT OF DISSERTATION

Title	Involvement of the OTUB1-YAP1 axis in driving malignant behaviors of head and neck squamous cell carcinoma (OTUB1-YAP1 経路の頭頸部扁平上皮癌の悪性化への関与)
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<p>Background: Comprehending the molecular mechanisms underlying head and neck squamous cell carcinoma (HNSCC) is vital for the development of effective treatment strategies. Deubiquitinating enzymes (DUBs), which regulate ubiquitin-dependent pathways, are potential targets for cancer therapy because of their structural advantages. Here we aimed to identify a potential target for HNSCC treatment among DUBs.</p> <p>Methods: A screening process was conducted using RNA sequencing data and clinical information from HNSCC patients in the TCGA database. A panel of 88 DUBs was analyzed to identify those associated with poor prognosis. Subsequently, HNSCC cells were modified to overexpress specific DUBs, and their effects on cell proliferation and invasion were evaluated. In vivo experiments were performed to validate the findings.</p> <p>Results: In HNSCC patients, USP10, USP14, OTUB1, and STAMBP among the screened DUBs were associated with a poor prognosis. Among them, OTUB1 showed the most aggressive characteristics in both in vitro and in vivo experiments. Additionally, OTUB1 regulated the stability and nuclear localization of YAP1, a substrate involved in cell proliferation and invasion. Notably, OTUB1 expression exhibited a positive correlation with the HNSCC-YAP score in HNSCC cells.</p> <p>Conclusions: This study highlights the critical role of OTUB1 in HNSCC progression via modulating YAP1. Targeting the OTUB1-YAP1 axis holds promise as a potential therapeutic strategy for HNSCC treatment.</p>	