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Report of "Research Award of Oral Sciences"

Major: Oral Sciences
Grade: 2
Department: Oral Bioscience
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Title: The role of deubiquitylation enzyme, OTUB1 in oral cancer development.

1. Aim of research and results obtained (Approximately 400 words):

Deubiquitinating enzymes (DUBs) comprise a large group of proteases which remove the ubiquitin(s) from the specific target proteins and regulate diverse ubiquitin-dependent pathways. By screening DUBs expression in head and neck squamous cell carcinoma (HNSCC) using The Cancer Genome Atlas (TCGA) database, I found OTUB1 (OTU deubiquitinase, ubiquitin aldehyde binding 1) is highly expressed in the primary HNSCC and significantly correlated with poor prognosis of HNSCC patients. The aim of this study is to clarify the role of OTUB1 in HNSCC.

First, the candidate genes which involved in the poor prognosis of oral cancer patients were screened from RNA-seq data of 519 primary HNSCC cases with the information of prognosis, obtained from TCGA database. Next, four types of DUB (OTUB1, USP10, USP14 and STAMBP) were transfected into HNSCC cell line, HSC2 by using lentiviral vector. To evaluate the candidate 4 DUBs' function, the assays of proliferation, invasion, and tumorigenesis were performed. Exosome was isolated from OTUB1-overexpressing cells and analyzed the containing proteins by Western blotting.

Based on the database screening, 4 candidates DUBs (OTUB1, USP10, USP14 and STAMBP) were selected. Among 4 candidates DUBs-overexpressing HSC2 cells, OTUB1-overexpressing cells showed the highest ability of proliferation and invasion. Moreover, we orthotopically injected 4 candidates DUBs-overexpressing HSC2 cells into the tongue of nude mice. After 4 weeks of orthotopic implantation, OTUB1-overexpressing cells showed aggressive tumors with lymph node and lung metastasis. Taken together, I concluded OTUB1 may have role to promote tumorigenesis and metastasis. Therefore, I focused on OTUB1 for further experiments.

Exosomes are membrane enclosed small vesicles comprising lipid bilayers and are mediators of intercellular communication that transport a variety of intracellular components. I isolated the exosome from OTUB1-overexpressing cells. Interestingly, ectopic OTUB1 and programmed death-1 (PD-L1) were detected in the exosome. As it recently has been shown that programmed death-1 (PD-L1) is a substrate of OTUB1, I make a hypothesis that exosome released from HNSCC cells with expression of OTUB1 and PD-L1 may transport ectopic PD-L1 via stabilizing ectopic OTUB1 to neighboring cancer cells for escaping immune response. Now I am performing further experiments to demonstrate my hypothesis.

2. Self-evaluation of research achievement:

After more than a year of research, I have made some achievements in Deubiquitinase OTUB1 in head and neck cancer. First of all, I found some phenotypes related to OTUB1. OTUB1 can promote the proliferation and invasion of head and neck cancer cells. In addition, when looking for the substrate of OTUB1, it was found that OTUB1 and PD-L1 could interact each other directly, and OTUB1 and PD-L1 existed in the exosome at the same time, which played an important role in mediating immune escape. In the past year, by reading the relevant papers on Deubiquitinase, I have a better understanding of this field, and mastered some important research methods of protein research, but the research process is still very slow. communication with professors and other members of the laboratory needs to be strengthened.

3. Meeting presentation:

* Title, conference, venue, date, co-author, presentation (oral/ poster).
(Underline the speaker.)

None

4. Journal publication:

* Title, journal, volume, number, paragraph, date, co-author.
(Underline the speaker.)

None