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Context specific role of deubiquitylase enzyme, USP9X in oral squamous cell carcinoma

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Oral squamous cell carcinoma (OSCC) represents one of the most common cancers in the world. Identification of oncogenes, onco-suppressors and their molecular mechanisms is necessary to understand the process of oral tumorigenesis. Recently, deubiquitylase enzyme, USP9X, has been implicated as a tumor suppressor in oral carcinomas. This study aimed to further investigate USP9X's role by knocking it down in four OSCC cell lines: SCC15, CAL27, FaDu and Detroit 562. Over 6 days all four cell lines displayed a reduction in cell numbers in the absence of USP9X and two of the cell lines, CAL27 and FaDu, revealed cell cycle alterations. USP9X regulates the mTOR pathway which plays a critical role in cell cycle progression. CAL27 and FaDu showed significant down regulation of the mTORC1 target, pS6 protein, in the absence of USP9X, probably causing the delay in cell cycle progression and decrease in cell numbers. In the other two cell lines, SCC15 and Detroit 562, differences in cell numbers were evident only after four days in culture. To determine if the delayed effect is due to terminal differentiation, levels of involucrin were assessed but no difference was observed. Interestingly, levels of MCL1, a pro survival protein and a USP9X substrate decreased in these cells after the fourth day. Hence the reduced cell numbers could be due to increased cell death. This study reveals that the absence of USP9X affects the proliferation/viability of OSCC cell lines. As previously shown, the roles of USP9X can be highly context specific and vary in early and advanced forms of oral cancers.

Biography

Devathri Nanayakkara is a final year PhD student from Eskitis Institute for Drug Discovery, Griffith University. She is working on the deubiquitylating enzyme, USP9X under the supervision of Dr Stephen Wood.

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