Deletion of LSD1 During Dysplasia Epigenetically Attenuates HNSCC Preneoplasia

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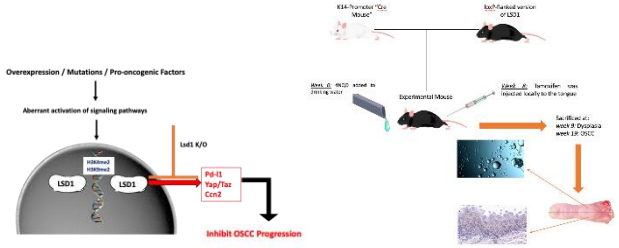
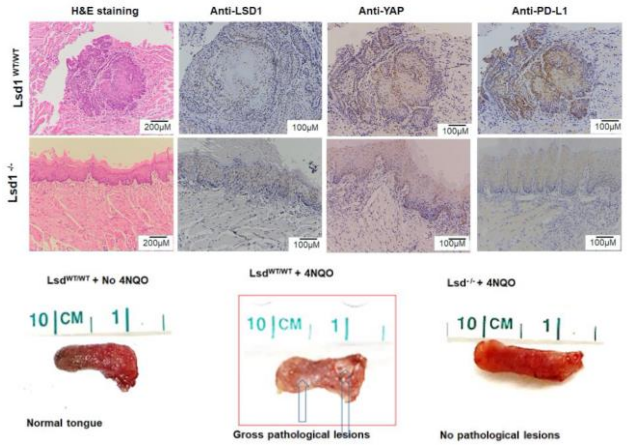
Introduction: Lysine Specific Demethylase (LSD1) functions as an epigenetic regulator and promotes cancer initiation, proliferation and metastasis. LSD1 expression has a high correlation in many solid tumors and is associated with poor outcomes of cancer.

Hypothesis: **We hypothesize that LSD1 regulates the development of OSCC.**

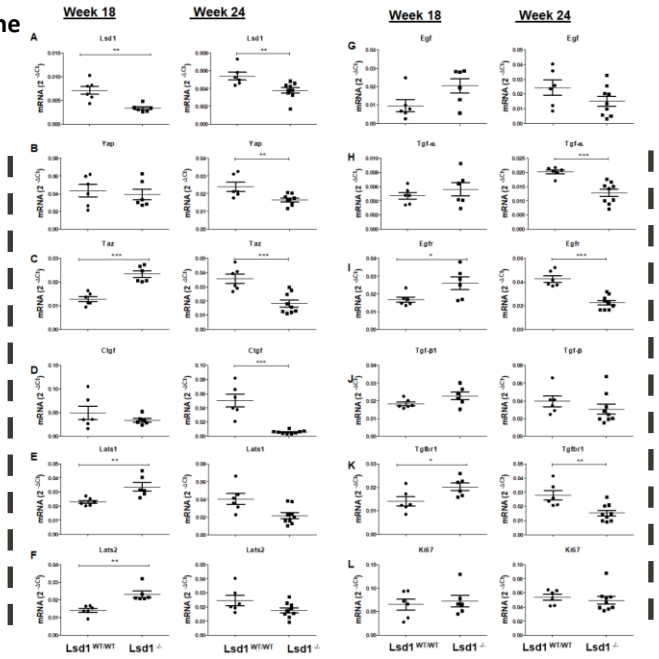
Rationale/Methods



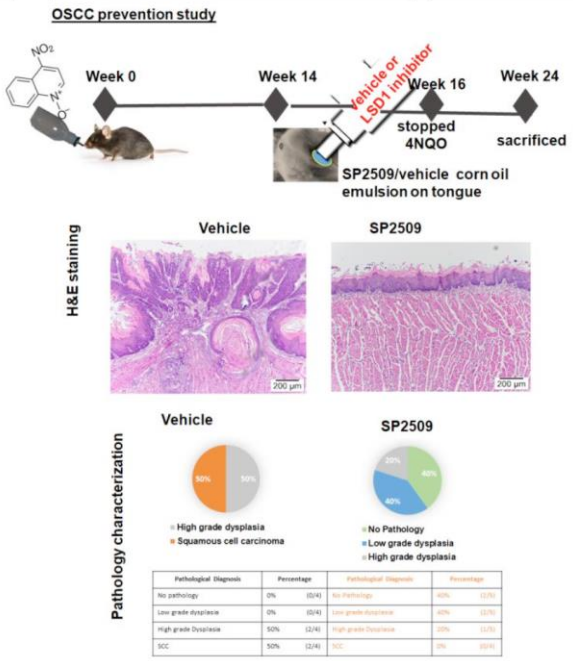
Lsd1 deletion reduces Lsd1, Pd-l1, and Yap expression in oral epithelium



LSD1 knockout in 4NQO OSCC mouse model regulated target gene expression in preneoplasia compared to OSCC



Topical application of LSD1 inhibitor SP2509 during dysplasia prevents progression of dysplasia to OSCC



Outcome and Conclusions

- Lsd1 deletion inhibits the development of squamous cell carcinoma in the tongue.
- Different genes are regulated depending on the stage of progression of cancer.
- Lsd1 is involved in the regulation of EGFR, TGF-β1, hippo and immune pathways.
- Lsd1 inhibitor attenuates the development of oral squamous cell carcinoma in 4NQO treated mice.

DScD project defended and manuscript submitted.

CITATIONS:

Alsaqer SF, Tashkandi MM, Kartha VK, Yang YT, Alkheriji Y, Salama A, Varelas X, Kukuruzinska M, Monti S, Bais MV. 2017. Inhibition of lsd1 epigenetically attenuates oral cancer growth and metastasis. Oncotarget. 8(43):73372-73386.

Bais MV, Kukuruzinska M, Trackman PC. 2015. Orthotopic non-metastatic and metastatic oral cancer mouse models. Oral Oncol. 51(5):476-482.

Kerenyi MA, Shao Z, Hsu YJ, Guo G, Luc S, O'Brien K, Fujiwara Y, Peng C, Nguyen M, Orkin SH. 2013. Histone demethylase lsd1 represses hematopoietic stem and progenitor cell signatures during blood cell maturation. Elife. 2:e00633.

Z. J. Lei, J. Wang, H. L. Xiao, Y. Guo, T. Wang, Q. Li, L. Liu, X. Luo, L. L. Fan, L. Lin, C. Y. Mao, S. N. Wang, Y. L. Wei, C. H. Lan, J. Jiang, X. J. Yang, P. D. Liu, D. F. Chen, B. Wang, Lysine-specific demethylase 1 promotes the stemness and chemoresistance of Lgr5(+) liver cancer initiating cells by suppressing negative regulators of beta-catenin signaling. Oncogene 34, 3188-3198 (2015).