

# Partial restoration of irradiation-damaged salivary function following Shh gene delivery

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Today at the 45th Annual Meeting & Exhibition of the American Association for Dental Research, researcher Fei Liu, Texas A&M Health Science Center, Temple, USA, will present a study titled "Partial Restoration of Irradiation-Damaged Salivary Function Following Shh Gene Delivery." The AADR Annual Meeting is being held in conjunction with the 40th Annual Meeting of the Canadian Association for Dental Research.

Irreversible hyposalivation is common in head and neck cancer survivors treated with radiotherapy. In this study, researchers found in a transgenic mouse model that transient activation of Hedgehog (Hh) pathway after irradiation (IR) rescued [salivary gland](#) dysfunction by preserving both salivary stem/progenitor cells and parasympathetic innervation. The researchers aimed to evaluate the effect of sonic hedgehog (Shh) gene transfer to murine submandibular glands (SMGs) on IR-induced hyposalivation and to further explore underlying mechanisms.

C57BL/6 mice received 15Gy single-dose IR with or without retrograde ductal instillation of adenoviral vectors encoding GFP or Shh (AdGFP or AdShh) on day 3 or 30 after IR. The progeny of cells responsive to Gli-dependent Hh pathway was traced in Gli1-CreER/Rosa26R mice after IR and/or AdShh treatment. The stimulated saliva flow rates in mice treated with AdShh on Day 60 and 90 were significantly increased compared to IR only or IR+AdGFP groups, but were still significantly lower than that in the non-IR group.

In SMGs collected on Day 90, AdShh significantly preserved the expression of acini marker Aqp5 and parasympathetic innervation marker Gfra2. AdShh also significantly ameliorated the vascular damage in irradiated SMGs as indicated by the expression of endothelial marker Aqp1 and the microvascular density, which is related to Gli-dependent upregulation of Angiopoietin-1/2. However, the progeny of cells responsive to Gli-dependent canonical Hh pathway was not significantly expanded by AdShh treatment after IR, suggesting that these cells might not function as stem/progenitor cells in SMGs after IR. Meanwhile, AdShh might activate some Gli-independent Hh pathways in SMGs that are harmful to the salivary gland function. Shh gene delivery partially restored salivary gland function after IR through preservation of parasympathetic innervation and microvascular endothelium.

This research suggests that inhibiting harmful responses to Hh activation in salivary gland may improve the efficacy of Hh-mediated rescue of IR-induced hyposalivation.

**More information:** This is a summary of oral presentation #0289, "Partial Restoration of Irradiation-Damaged Salivary Function Following Shh Gene Delivery," which will be presented on Thursday March 17, 2016, 11:30 a.m. - 11:45 a.m. at the Los Angeles Convention Center, room #406A.

Provided by International & American Associations for Dental Research

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