

3rd International Conference and Exhibition on Cell & Gene Therapy

October 27-29, 2014 Embassy Suites Las Vegas, USA

Retrograde salivary gland ductal delivery of the adenovirus-mediated *NDRG2* gene: A potential therapeutic method for estrogen-deficient xerostomia

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Xerostomia is a subjective symptom and prevalent in more than one-third of postmenopausal women who usually complaint of seriously interfered chewing, deglutition, and speaking. Saliva production is subjected to the processes of a plasma-like, isotonic primary secretion in salivary acini and subsequent re-absorption of Na⁺ and Cl⁻ in the collecting ducts, leaving hypotonic saliva into the oral cavity. Some xerostomia patients actually do not suffer from decreased saliva secretion but from the increased ionic osmotic pressure or viscosity of saliva. Although the feeling of oral dryness can be ameliorated with estrogen supplementation administration, the side effects of estrogen greatly restrict its application. We found that N-myc downstream regulated *gene 2* (*NDRG2*) is involved in estrogen-mediated Na⁺ and Cl⁻ transport in salivary ductal cells. In addition, an ovariectomized rat model was used to mimic xerostomia in postmenopausal women and adenovirus vectors bearing *NDRG2* were constructed to validate their therapeutic potential. Ovariectomized rats exhibited severe sialaden hypofunction, including decreased saliva secretion and ion re-absorption, as well as increased water consumption. It was also found that the expression of *NDRG2*, Na⁺/K⁺-ATPase, and epithelial sodium channels (EnaC) decreased in ovariectomized rat salivary glands, which are all involved in Na⁺ re-absorption. Retrograde ductal delivery of *NDRG2* adenovirus in ovariectomized rat through submandibular gland can efficiently improve the dysfunction of Na⁺ and Cl⁻ re-absorption, and promote saliva flow rate and water intake return to normal levels. This study elucidates the underling mechanism of estrogen deficiency-mediated xerostomia and provides an attractive strategy for therapeutic intervention.

Biography

Yan Li has completed her PhD from the Fourth Military Medical University (China) in 2009 and she used to be a Visiting Scholar for Post-doctoral research in Purdue University (USA). Now she is a Lecturer of the Department of Biochemistry and Molecular Biology, the Fourth Military Medical University (China). She has published more than 30 papers in reputed journals, including *J BiolChem*, *MolTher*, *Breast Cancer Res*, and *Cell Death Dis*.

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