Dysfunction of salivary glands underlying xerostomia and treatments

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In rat parotid acinar cells under control conditions, most of the aquaporin-5 (AQP5) is localized in the cytoplasm in a net-like shape, although some of it is present in the apical plasma membrane (APM). From 3 to 10 min after cevimeline-injection, AQP5 immunofluorescence was predominantly associated with the APM, and some AQP5 had trafficked to the nuclei. Subsequently, the AQP5 was internalized to the cytoplasm from the APM and gave rise to buds together with lipid rafts. AQP5 was recognized in isolated nuclei 3 min after cevimeline injection, but not under control conditions. Atropine induced not only an increased distribution of AQP5 in a diffuse pattern within the cytoplasm, but it also decreased the responsiveness of AQP5 to cevimeline. Upon activation of M3 mAChRs, AQP5 was dramatically trafficked to nuclei and then the APM, along with lipid rafts.

Acethycholine (ACh) increased the amount of AQP5 on the APM by 3.6-fold, but 1.8-fold in those of senescent rats. The translocation of AQP5 was decreased during, however, cevimeline induced a persistent increase in AQP5 amounts on the APM in the glands of both these rats. Although the level of AQP5 mRNA in the parotid glands of streptozotocin-induced diabetic rats was 2.5-fold higher than that of control rats, protein synthesis for AQP5 was decreased. Twelve hours after intraperitoneal injection of insulin, the level of AQP5 mRNA was decreased. In addition, the response of AQP5 sorting to apical membranes to cevimeline was also reduced in diabetic rats. Administration of insulin to diabetic rats restored the cevimeline-induced trafficking of AQP5 as observed in control rats. Therefore, evimeline is a useful tool for the cure of xerostomia caused by aging or diabetes.