EXPANDED ABSTRACT

Anion secretory functions of acinar and intralobular duct cells in the rat parotid gland

Chikara Hirono, Makoto Sugita, Yoshiko Iwasa, and Yoshiki Shiba

Department of Oral Physiology, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan

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To clarify difference of anion secretory function between acinar and intralobular duct cells in the rat parotid gland, we investigated anion currents with the gramicidin-perforated patch recording method. Anions are supplied only by the cells themselves and released through anion channels in the gramicidin-perforated patch configuration. Accordingly, the anion currents measured with the present method reflect the anion-supplying activity and the anion channel activity of the cells (1). Furthermore, anion conductance, which reflects the anion channel activity, can be measured by superimposition of brief 5 mV pulses on the holding potential separately from anion currents. Thereafter the driving force, which reflects intracellular anion concentration, can be estimated.

In the acinar cells, carbachol (CCh), a Ca^{2+}-increasing agent, induced an oscillatory anion current, of which amplitude became rather steady in 5 min after the CCh addition. cAMP-increasing agents, isoproterenol (IPR) and forskolin, evoked no marked current and reduced the CCh-induced oscillatory current (2). Bumetanide suppressed the CCh-induced oscillatory current in the steady state, suggesting that the oscillatory current in the steady state is driven mainly by Cl^- uptake activity of the Na^+-K^+-$2Cl^-$ cotransporter. Superimposition of brief 5 mV pulses on the holding potential, −80 mV, under the suppression of K^+ channels by blockers revealed that anion conductance was oscillatory. The Ca^{2+} ionophore, A23187, induced a nonoscillatory inward current in the acinar cells. The A23187-induced current and the driving force in the steady state were bumetanide-sensitive, but membrane conductance was not very sensitive to bumetanide. These are consistent with the effect of bumetanide on the CCh-induced oscillatory current.

In the intralobular duct cells, both CCh and IPR induced nonoscillatory currents with nonoscillatory increases in membrane conductance. The Ca^{2+} ionophore, A23187, mimicked the CCh-induced current and the A23187-induced current in the steady state was blocked by diphenylamine-2-carboxylate. Forskolin mimicked the IPR-induced current and the forskolin-induced current in the steady state was sensitive to glibenclamide (3) and $CFTR_{inh}$-172. All these currents during the steady state were inhibited by HCO_3^- removal and addition of methazolamide and 5-(N,N-dimethyl)amiloride (DMA). The driving force, estimated from currents and membrane conductance, was sensitive to methazolamide and DMA, but membrane conductance was not. These suggest that the duct cells secrete HCO_3^- with coordinated activities of the carbonic anhydrase and the Na^+-H^+ exchanger, through a kind of Ca^{2+}-depedent Cl^- channel and the CFTR Cl^- channel activated by Ca^{2+} and cAMP signals, respectively.

We conclude that Cl^- secretion in acinar cells depends on an oscillatory increase in anion conductance and the driving force produced by the Na^+-K^+-$2Cl^-$ cotransporter during the Ca^{2+} signaling, while HCO_3^- secretion in intralobular duct cells is maintained by nonoscillatory increases in anion conductance and the driving force generated by the carbonic anhydrase with the support of the Na^+-H^+ exchanger during both Ca^{2+} signaling and cAMP signaling.

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Address correspondence and reprint requests to Chikara Hirono, Department of Oral Physiology, Hiroshima University Graduate School of Biomedical Sciences, 2-3, Kasumi 1-Chome, Minami-ku, Hiroshima 734-8553, Japan and Fax : +81-82-257-5627.

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