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Localization, activation and deactivation of Ca^{2+} dependent Cl^- channels in pancreatic acinar cells

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In exocrine acinar cells, Ca^{2+}-activated Cl^- channels in the apical membrane are essential for fluid secretion, but it is unclear whether such channels are important for Cl^- uptake at the base. Whole cell current recording, combined with local uncaging of caged Ca^{2+}, was used to reveal the Cl^- channel distribution in mouse pancreatic acinar cells, where ~90% of the current activated by Ca^{2+} in response to acetylcholine was carried by Cl^-. When caged Ca^{2+} in the cytosol was uncaged locally in the apical pole, the Cl^- current was activated, whereas local Ca^{2+} uncaging in the basal or lateral areas of the cell had no effect. Even when Ca^{2+} was uncaged along the whole inner surface of the baso-lateral membrane, no Cl^- current was elicited. There was little current deactivation at a high cytosolic Ca^{2+} concentration ($[Ca^{2+}]_c$), but at a low $[Ca^{2+}]_c$ there was clear voltage-dependent deactivation, which increased with hyperpolarization. Functional Ca^{2+}-activated Cl^- channels are expressed exclusively in the apical membrane and channel opening is strictly regulated by $[Ca^{2+}]_c$ and membrane potential. Ca^{2+}-activated Cl^- channels do not mediate Cl^- uptake at the base, but acetylcholine-elicited local $[Ca^{2+}]_c$ spiking in the apical pole can regulate fluid secretion by controlling the opening of these channels in the apical membrane.