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Title: Sodium transport mediated by concentration-sensitive sodium channel in mouse alveolar epithelium

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Body: Introduction: The concentration-sensitive Na^+ channel (Na_C), a member of the family of voltage-dependent Na^+ channels, opens in response to increased Na^+ concentration in the extracellular fluid ($[Na^+]_o$). Although the expression of Na_C in alveolar epithelial type II (AT II) cells has been reported, the physiological role of Na_C in lung tissue has not yet been established. Various ion channels in the alveolar epithelium are involved in maintaining the alveolar fluid balance; therefore, we hypothesized that Na_C-mediated Na^+ transport contributes to the clearance of Na^+ from the alveolar fluid. In this study, we examined Na_C distribution in mouse lung tissue and the $[Na^+]_o$-dependent influx of Na^+ into mouse alveolar epithelium. Methods: We used immunohistochemistry and immunofluorescence to study mouse lung tissue using antibodies against Na_C and other ion transport proteins. In situ hybridization was performed using a digoxigenin-labeled antisense probe for Na_C mRNA. Na^+ dynamics in mouse alveolar epithelium were analyzed using sodium-binding benzofuran isophthalate and an image analyzer Argus-50. Results: The alveolar epithelial type I (AT I) cells showed positive staining with anti-Na_C antibodies. Similarly, Na_C mRNA signals were detected in the AT I cells by in situ hybridization. Confocal laser scanning microscopy showed the presence of Na_C in the cell membrane of the AT I cells. Na_C was partially colocalized with γ epithelial sodium channels (ENaC). Results of image analysis showed that Na^+ influx into alveolar epithelium was dependent on elevation of $[Na^+]_o$. Conclusions: These findings suggest that Na_C, expressed in AT I cells, is involved in Na^+ transport in the alveolar epithelium.