In the course of my PhD thesis I was able to demonstrate, that incorporation of the atypical delta-subunit (δ) into epithelial sodium channels (ENaC) from *Xenopus laevis*, removes channel regulation by proteolysis while introducing a profound sensitivity for extracellular protons. Expression of δ-ENaC in the kidney and urinary bladder of the pipid frog may indicate a functional interconnection between luminal Na⁺ absorption and acid-secretion in epithelia lining the urinary excretory tract. Distinct regulatory properties of ENaC isoforms in *Xenopus laevis* potentially enable functional discrimination of channel subpopulations in native amphibian tissues and thereby could provide insight into the controversial physiological significance of δ-ENaC in vertebrates. Future studies may also aim to identify the molecular determinants of ENaC regulation by the extracellular pH and proteases in order to understand how constitutive ENaC activity emerged from a family of stimulus-activated ion channels. Furthermore, comparative physiological approaches might elucidate if and how ENaC-mediated transepithelial Na⁺ absorption aided in the environmental adaptation of vertebrates facing osmotic challenges during water-to-land transition.