The receptor function of the hair cells requires a high [K+] in the endolymph and a positive endolymphatic electrical potential. Both are generated by K+ transport by the stria vascularis and depend on an intact gap-junctional system. Gap junctions are an important component of the complex system responsible for the generation of an endolymphatic fluid with high [K+] and probably the endolymphatic electrical potential. In addition, there is a role of gap junctions in the recycling of the K+ that enters the hair cells from the endolymph, back into that space. Activation of the hair cells by sound waves results in opening of non-selective cation channels near the tips of the stereocilia, eliciting influxes of Ca2+ and K+ and membrane depolarization. The K+ that enters the hair cells moves across their basolateral membrane into the perilymphatic space between the hair cells and supporting cells (cortilymph). Most likely, this K+ is taken up by the supporting cells and recycled back into the endolymph via the cochlear gap-junctional network. Mutations of Cx26 can therefore affect the ionic homeostasis of the organ of Corti by reducing or preventing K+ recycling. Alternatively, connexin mutants may still form channels permeable to K+, but may show more subtle permeability changes, brought about by a decrease in pore size or changes in charge selectivity. In this case, the mutations would not affect K+ recycling in the cochlea, but may affect cell function by altering second-messenger transport between cells. The Cx26 V84L mutant forms GJC permeable to small inorganic ions, but displays reduced permeability to IP3.

Gap-junctional networks and K+ recycling in the cochlea. A. Schematic cross-section of the cochlea. B. Schematic view of the cochlea focused on the gap-junctional networks and their proposed role in K+ recycling. A and B are adapted from Kikuchi et al. and Steel.