Na+ current properties in islet β- and α-cells reflect cell-specific Scn3a and Scn9a expression.

Abstract:
Mouse pancreatic β- and α-cells are equipped with voltage-gated Na(+) currents that inactivate over widely different membrane potentials (half-maximal inactivation (V0.5) at -100 mV and -50 mV in β- and α-cells, respectively). Single-cell PCR analyses show that both β- and α-cells have Nav1.3 (Scn3) and Nav1.7 (Scn9a) β subunits, but their relative proportions differ: β-cells principally express Nav1.7 and α-cells Nav1.3. In β-cells, genetically ablating Scn3a reduces the Na(+) current by 80%. In α-cells, knockout of Scn9a lowers the Na(+) current by >85%, unveiling a small Scn3a-dependent component. Glucagon and insulin secretion are inhibited in Scn3a(-/-) islets but unaffected in Scn9a-deficient islets. Thus, Nav1.3 is the functionally important Na(+) channel β subunit in both β- and α-cells because Nav1.7 is largely inactive at physiological membrane potentials due to its unusually negative voltage dependence of inactivation. Interestingly, the Nav1.7 sequence in brain and islets is identical and yet the V0.5 for inactivation is >30 mV more negative in α-cells. This may indicate the presence of an intracellular factor that modulates the voltage dependence of inactivation.