Ion channel regulation by \(\beta\)-secretase BACE1 - enzymatic and non-enzymatic effects beyond Alzheimer's disease.

?-site APP-cleaving enzyme 1 (BACE1) has become infamous for its pivotal role in the pathogenesis of Alzheimer's disease (AD). Consequently, BACE1 represents a prime target in drug development. Despite its detrimental involvement in AD, it should be quite obvious that BACE1 is not primarily present in the brain to drive mental decline. In fact, additional functions have been identified. In this review, we focus on the regulation of ion channels, specifically voltage-gated sodium and KCNQ potassium channels, by BACE1. These studies provide evidence for a highly unexpected feature in the functional repertoire of BACE1. Although capable of cleaving accessory channel subunits, BACE1 exerts many of its physiologically significant effects through direct, non-enzymatic interactions with main channel subunits. We discuss how the underlying mechanisms can be conceived and develop scenarios how the regulation of ion conductances by BACE1 might shape electric activity in the intact and diseased brain and heart.