Abstract

Rhythmic activity of single cells or cellular networks is a common feature of most organisms. Cellular rhythms govern the beating of the heart, cycles of sleep and wakefulness, breathing, and the release of hormones. The endogenous rhythmic activity of many neurons and cardiac relies on a complex interplay between several distinct ion channels. In particular, one type of ion channel plays a prominent role in the control of rhythmic electrical activity because it determines the frequency of the oscillations. The activity of the channels is thus setting the "pace" of the activity; therefore, these channels are often referred to as "pacemaker" channels. Despite their obvious physiological importance it hasn´t been until a few years ago that the genes encoding pacemaker channels have been identified. Because both hyperpolarization and cyclic nucleotides are key elements that control their activity, pacemaker channels have now been designated hyperpolarization-activated and cyclic nucleotide-gated (HCN) channels. From a scientific as well as medical point of view, HCN channels are interesting drug targets. Only a few substances are known that specifically affect HCN channels. In the present study, a microtiter plate-based high throughput screening assay for HCN1 and HCN4 channels was developed. With this assay, known drugs for HCN channels were characterized. Subsequently, venoms of snails, spiders, scorpions, and snakes were screened for toxins affecting HCN channel activity. A few venoms were identified that possibly contain drugs that act on HCN channels.