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TRP-ing the light fantastic: Activation of TRPC5 and other channels using internal perfusion on an APC platform

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Ion channels have been recognized as an important therapeutic target class for treating a number of different pathophysiologies. This target class is becoming even more important as the personalized medicine revolution evolves. However, a major limiting factor in the drug discovery process involving ion channels is the technically demanding electrophysiological assay which remains the gold standard since its discovery in the 1970's. Although automated patch clamp instruments have been successfully introduced in recent years, none of them combine the quality and flexibility of manual patch clamp with the throughput required for true high throughput screening (HTS) efforts. We present data on Nanion's SyncroPatch 384PE which is a high throughput giga-seal platform recording up to 768 experiments simultaneously. Using this system, biophysical properties of the ion channel can be studied and coupled with reliable pharmacology and complex effects of compounds. We show state dependent effects of tetracaine on NaV1.7. Additionally, a number of different TRP channels and chloride channels are activated by internal calcium. Furthermore, we show activation of TRPC5 and TMEM16A by perfusion of intracellular Ca²⁺ and inhibition by external application of compounds.