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Player (Chup Chup Ke
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Download)A cellular
biological method of
analyzing and
quantitating ion
channel gating. Ion
channels control many

vital and disease-causing processes in cells. Previous methods of analyzing ion channel gating are limited in that they are typically qualitative and require multiple assumptions and

measurements. These difficulties have limited attempts to quantify the molecular mechanisms of ion channel gating. Here we describe a novel cellular-based approach to assess the gating of

individual ion
channels. This method
utilizes whole-cell
recording of
membrane potential,
with a standard
bathing solution, in
the presence and
absence of
pharmacological tools,

to analyze the gating behavior of the channels (voltage-gated and ligand-gated) in the cell being studied. We demonstrate this method on six different ion channels (Ca(V)1.2, Ca(V)1.3,

Ca(V)1.4, Ca(V)2.1,
Kv1.2, and Kv1.3)
expressed in two
different cell types.

We further
demonstrate the
utility of the method
by examining the
properties of T-type
calcium channels

expressed in HEK293 cells. We found that the kinetics of inactivation and activation of the channels were not identical in HEK cells and normal rat cardiomyocytes. This result can be

interpreted in terms of differences in cell-specific factors, such as voltage-gated currents in the two cell types. Thus, this approach is a highly flexible technique for quantitatively analyzing the

behavior of ion channels expressed in any cell type. In principle, this approach is applicable to any voltage-gated ion channel. Some pathological states of the human body may be caused, or

accompanied, by build-up of toxins in tissues and consequent accumulation of toxic metabolites in blood and other body fluids.

The ability to effectively detoxify body fluids and tissues could be a

pivotal factor in
preventing the
progression and
severity of certain
pathological states.

For example,
excessive
accumulation of
ammonia in body
fluids such as blood,

urine, cerebral spinal fluid and the like can cause or exacerbate a number of pathological conditions. Arterial and venous blood in the brain have pH values in the range 6.8-7.2, and cerebral

spinal fluid has a pH value of about 8.7. The blood pressure in the brain creates a hydrostatic pressure gradient that drives fluid in these regions through the aquaporins that are present in the

capillary membranes
of the cerebral
microvasculature. In
the presence of a
blood-borne toxin,
e.g., ammonia, excess
water moves from the
blood into the brain,
thereby diluting the
blood and raising its

pH. However, once the blood reaches brain tissue, the movement of water into the tissue is opposed by a finite capillary surface area.

As a result, the pressure gradient will tend to drive more

fluid into the brain,
resulting in an influx
of blood into brain
tissue and a rapid
build-up of ammonia.
This builds the risk of
an ammonia coma,
and also worsens the
risk of thiamine
deficiency in the

hypothalamus,
resulting in Wernicke
encephalopathy,
which in turn leads to
further tissue
damage. 5ec8ef588b

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